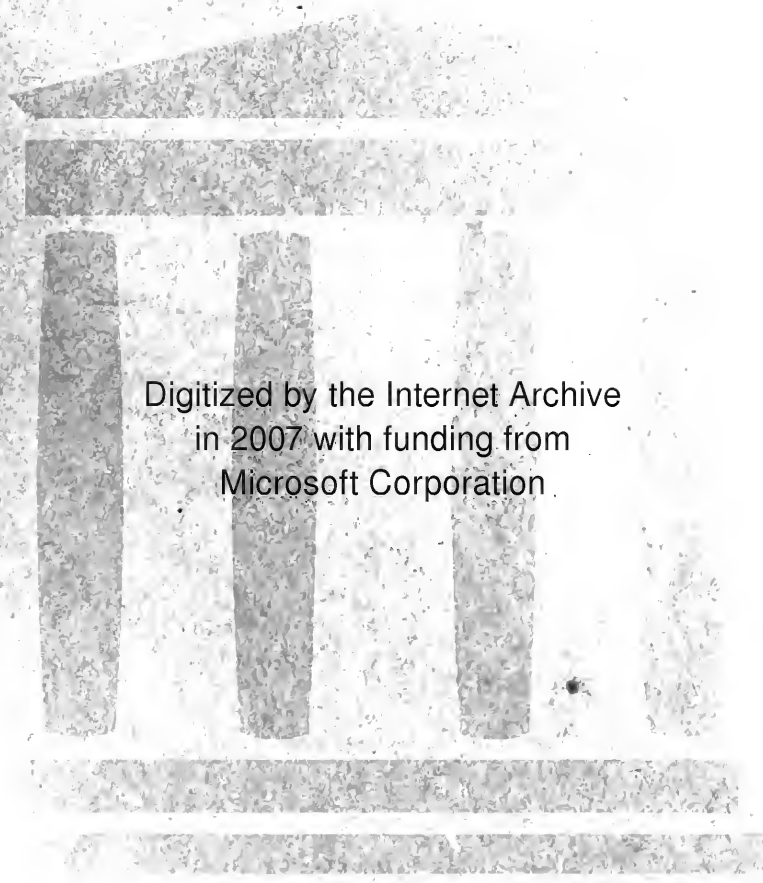




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PELVIC NEOPLASMS

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BY

FRANK WORTHINGTON LYNCH, A.B., M.D.

PROFESSOR OF GYNECOLOGY AND OBSTETRICS, UNIVERSITY OF CALIFORNIA;
DIRECTOR OF WOMAN'S CLINIC, UNIVERSITY OF CALIFORNIA HOSPITAL

AND

ALICE F. MAXWELL, B.S., M.D.

INSTRUCTOR IN GYNECOLOGY AND OBSTETRICS, UNIVERSITY OF CALIFORNIA;
ATTENDING GYNECOLOGIST AND OBSTETRICIAN,
UNIVERSITY OF CALIFORNIA

↓
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PREFACE

IN this volume, the authors have attempted to present the important features of pelvic neoplasms from data obtained by a critical survey of the literature and from personal observations.

Since malignant tumors form a large proportion of these pelvic new-growths, their early symptoms, appearance and diagnosis have been emphasized. As long as the etiology and prophylactic measures for cancer remain unknown, this emphasis appears merited.

It has been our aim to make the monograph of practical value and considerable space has been given to treatment. In the years which have elapsed since the preparation of a similar volume, the advantages and disadvantages of surgical treatment of malignant pelvic tumors have been definitely ascertained. Radium, on the contrary, is a relatively recent addition to our therapeutic armamentarium. While conclusions as to its usefulness and value in comparison with surgery may not be definitely drawn, we must not overlook its possibilities. We have, therefore, devoted considerable space to this subject. Theoretical discussions have been included only to clarify the subject matter or to indicate various avenues for scientific research.

The authors acknowledge with gratitude the aid afforded by Dr. Margaret Schulze, amounting nearly to co-authorship, in review of the literature and the preparation of the chapter on Mammoth Ovarian Tumors; to Dr. Howard Kelly for his generous permission to use many drawings which have illuminated his own texts; and to Miss Elizabeth Coats for preparation of the manuscript. They also acknowledge their appreciation of the drawings of Mr. Ralph Sweet, who made the original sketches from material in the Gynecological Laboratory of the University of California Medical School.

THE AUTHORS.

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PELVIC NEOPLASMS



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CHAPTER I

BENIGN TUMORS OF OUTLET

Fibroma of vulva—Classification—Etiology—Appearance and size—Degenerations—Symptoms—Diagnosis—Treatment—Literature—Lipoma of vulva—Etiology—Location and appearance—Rate of growth—Symptoms—Diagnosis—Treatment—Literature—Sweat gland tumors—Classification—Etiology—Histology—Size, appearance and location—Symptoms—Question of malignancy—Diagnosis—Treatment—Literature—Cysts of hymen—Frequency—Size and appearance—Histology—Etiology—Symptoms—Treatment—Other benign tumors.

FIBROMA OF THE VULVA

Fibroma of the vulva is the most common of the solid benign tumors in this region, yet its rarity is shown by the fact that there are less than 175 cases reported in the literature. Since many men have observed cases which have not been recorded, the comparative infrequency of the growth may be shown better by Leonard's report of only six fibroid tumors of the vulva found in 23,000 gynecological admissions to the Johns Hopkins Hospital. We have met with only one case in the last 1,200 gynecological cases at the University of California hospitals.

Classification.—Under the general heading of fibroma of the vulva are grouped not only the various fibroids which develop in that structure, but also the fibroids which develop elsewhere, and which later in their growth find their way by extension into the vulva. Naturally the great majority of the latter group have originated in the round ligament. A considerable number have developed from connective tissue deeper in the pelvis. This classification, while not correct at first sight, has the justification that the great majority of tumors of the round ligament develop in the extra-peritoneal portion of the structure and are forced outward as they grow. Thus Emanuel, in 1903, states that of his 80 cases of tumors of the round ligament only 20 developed intra-abdominally, while the other 60 were found either in the inguinal canal or in the labia. In the same manner, the tumors which develop from the pelvic fascia and deep connective tissue find their way through the natural planes of cleavage to the external genitalia. This classification, therefore, seems rational for the purposes of the present chapter.

Comparatively few men in recent time have reviewed the literature. Supplemental to Emanuel, Taussig, in 1914, presented his study of tumors of the round ligament and collected 90 extra-abdominal cases which he presented as vulvar growths. Later, in 1917, Leonard tabulated 131 cases of vulvar fibroids collected from the literature, although it appears that several cases cited by Emanuel and Taussig are not included in the compilation. We quote Leonard's table, not only to show the various points of origin of the growths classed as vulvar fibroids, but also to show the relative frequency of the various types which have been encountered.

Leonard's table.—

1. Fibroid tumors originating in the subcutaneous connective tissue . . . 70 cases.

(a) Labium majus.....	53 cases
(b) Labium minus.....	11 cases
(c) Vestibule and vagina.....	5 cases
(d) Perineum	1 case

2. Fibroid tumors originating in the extraperitoneal portion of the round ligament . . . 39 cases.

(a) Growing outward into the labium.....	25 cases
(b) Remaining within the canal.....	11 cases
(c) Growing backward into the abdomen.....	2 cases
(d) Growing up between the layers of the abdominal wall.	1 case

3. Fibroid tumors originating in the subperitoneal connective tissue and appearing at the vulva . . . 14 cases.

4. Fibroid tumors originating in the connective tissue of Bartholin glands . . . 2 cases.

5. Fibroid tumors originating in hematoma . . . 2 cases.

6. Fibroid tumors originating in the connective tissue of the recto-vaginal septum . . . 2 cases.

Etiology.—The etiology is not known. As shown in the classification cited above, the tumors may develop from the subperitoneal connective tissue, the extraperitoneal portion of the round ligament, connective tissue of muscle fibers of the vulva and perineum. Some, as Morestin, have advanced the view that a fibroma may develop during the organization of a hematoma. Kewisch claimed that they may arise from either the pelvic fascia or the periosteum of the pelvic bones; and Fromme, von Recklinghausen and others hold that they could originate in the connective tissue of Bartholin's gland. Others, as Taussig, with whom we agree, hold that the great majority of these tumors spring from structures of the round ligament, and that many of the glandular tumors of earlier times would have been diagnosed at present as adenomyoma.

Trauma has been advanced as a predisposing factor, especially in the cases which first presented as hernias and which wore trusses. While this view cannot be denied, it seems more likely that the supposed hernias were in reality tumors in their earlier stages which were stimulated to more rapid growth by pressure of the trusses.

More striking is the fact that nearly all of these tumors occur in women during the child-bearing age, the great majority of them being between the ages of 25 and 38. The tumors may, however, develop after the menopause, and Esser, Polaillon, Weber, and many others have presented

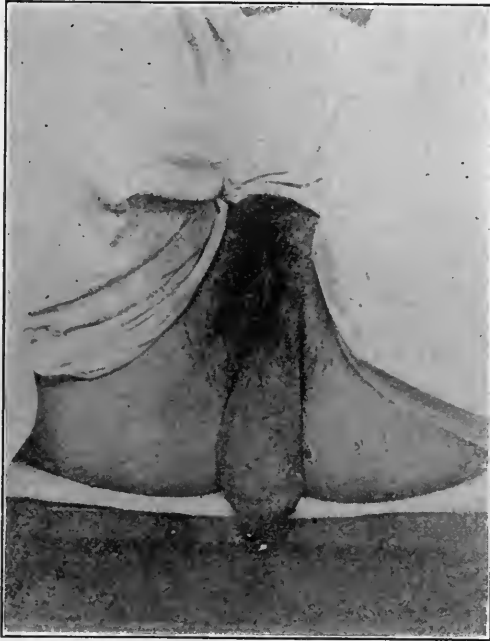


FIG. 1.—FIBROMA OF THE LABIUM MAJUS RESEMBLING SCROTUM (Leonard).

examples. Von Winckel's round ligament tumor was found in a woman of 76. On the contrary, Aichel, in 1912, noted one in a newly born child, and Goldreich, in 1909, described a pedunculated fibroid on the labium of a nursing infant.

Appearance and Size.—The tumor usually appears as a small, firm, smooth, round or oval nodule immediately under the skin of the labia, under which it moves freely. Occasionally it is multilocular. There may be multiple growths. The overlying skin is generally thick, and in the resting periods of the tumor's growth is frequently thrown into shallow folds suggesting the scrotum. The remarkable resemblance which the nonpedunculated tumors of the labium majus bear to the scrotum (Fig. 1) is frequently commented upon in the literature. The smaller tumors are generally either contained in the labia or have a sessile base. Later in their

growth they (especially the tumors arising below the inguinal ring) develop a pedicle which may be of considerable length (Fig. 2). Both the tumors and the stalk of the growths arising in the labium majus are frequently covered with hair.

Not all tumors, however, present this rather characteristic appearance. Occasionally some present an entirely different appearance, as did the case of Kirchoff. This tumor was projected from the vagina of a girl of eighteen years, when it was found to be an ulcerated, edematous, hemor-



FIG. 2.—FIBROMA OF LABIUM MAJUS WITH WELL-DEVELOPED PEDICLE (Leonard).

rhagic mass of fibrosarcomatous nodules attached by a broad pedicle to the right labium minus (Fig. 3).

Tumors which begin in the inguinal canal often dissect their way upwards between the layers of the abdominal wall and form masses which at first sight are considered intraperitoneal neoplasms. The tumors are usually firm, although many present a semisolid or even fluctuating consistency as a result of edema or of sarcomatous changes. Even the solid tumors give an altered feel when the patient is menstruating, because of the alterations in the circulation of the growth at that time. Penrose states that they may swell to twice their usual size during the menstrual period and return soon after to their former size and firm consistency. Many have emphasized the fact that the growth also becomes soft and semifluctuant during pregnancy, during which time it grows with astonishing rapidity,

doubtless from processes similar to those which occur in uterine fibroma during pregnancy. The folds and wrinkles in the skin become obliterated from edema so that the skin surfaces surmounting the tumor are smooth and shiny. Ulcerations frequently appear at that time and soon become infected. When the tumor presents sarcomatous changes, ulceration is extremely common.

Emanuel found that the great majority of his collected cases were on the right side, but later compilers have not noted similar results.



FIG. 3.—FIBROID OF LABIUM WITH SARCOMATOUS DEGENERATION (redrawn from Kirchoff).

The size of the growths varied greatly, ranging from small nodules to tumors of enormous size. Perewaloff described a 31-pound tumor mass of the labium majus which hung from its pedicle down to the knees. Grimes removed a sloughing mass of similar location which weighed 16½ pounds. The great majority of labial tumors, however, are smaller, averaging the size of a hen's egg. Tumors of the labium minus are generally smaller. Grigorowitsch's case appears to be the largest, a number of small tumors surrounding a mass which weighed 740 grams.

Tumors which originate in the submucous connective tissue of the vesti-

bule and vagina are usually small, yet the fibroid reported by Newman grew from the perineum and was the size of a fetal head.

The subperitoneal fibroma is more uniformly of large size and more likely to be multiple (Fig. 4). Esmarch records a case of a woman of thirty who presented simultaneously a pedunculated tumor of the right labium the size of a child's head; a pedunculated mass hanging from the right buttock the size of a man's head; and a fist-sized tumor in the right inguinal region. Gallet's case is also worth citing. A woman of thirty-eight with a large tumor of the left labium majus; a tumor of the size of a man's head on the left buttock; and just above it a smaller tumor of the same nature. At



FIG. 4.—PEDUNCULATED MULTIPLE FIBROMA.

operation, the vulvar tumor was found to spring from a pedicle which continued up beneath the ramus of the pubes. The smaller tumor of the buttocks hung from a pedicle coming out of the obturator foramen. The patient died, and, at autopsy, the pedicles of all three tumors were found to connect with a similar tumor which was not connected with the pelvic organs in any way. The tumors were fibromatous, containing many cystic cavities.

Buckner's case, described in 1851, is of striking interest in that the tumor masses were estimated to weigh 268 pounds, which, with the possible exception of Spohn's and Barlowe's mammoth ovarian tumors, is the largest neoplasm of which we have record (Fig. 5). While the details of this case are not entirely clear, it is of sufficient interest to warrant the quotation of Buckner's notations.

In 1843, a married woman, aged twenty-five years, gave birth to a still-born child at term. This was her fourth pregnancy. Following it there was difficulty in passing urine, and the catheter was used for some months. At this time a soft, immovable tumor was felt a little to the right of the linea alba, almost filling the right side of the abdomen. It increased rapidly. Four years later (1847), another tumor appeared in the right labium extend-



FIG. 5.—MAMMOTH FIBROMA (drawn from Buckner's daguerreotype).

ing to the nates. It was soft and elastic, and for a year or two could be returned to the abdomen. It subsequently enlarged as the abdominal tumor did, and fluctuated so distinctly as to be mistaken for a case of dropsy. These tumors were tapped or incised eight times, but no fluid was discharged. The growth caused most distressing symptoms, and the patient could hardly breathe except upon her hands and knees. But with the enlargement of the tumor of the buttock, the dyspnea was relieved as well as a general anasarca and numbness of the legs. At the request of the

patient this growth was opened and the finger introduced, but a soft tissue, like the omentum, was all that could be felt.

A year later (1848) she became pregnant again, and was delivered at full term, by artificial means, of a child which died during labor. It must have been indeed a case of "*mons laborat*," and many difficulties must have been surmounted at the time of conception, for it is stated that before this last pregnancy, when she was in a sitting posture, which she sometimes attempted, the abdominal tumor rested upon her thighs as far as her knees, and the tumor of the hip was fifteen inches long, ten inches in greatest diameter and four inches at the point of its connection with the perineo-ischiatic region.

In 1850, two years later, the patient weighed 269 pounds. As her greatest weight before marriage was 108 pounds, and as her flesh was greatly reduced, it was estimated that the entire growth was about 180 pounds.

In 1851, Dr. Buckner traveled 220 miles to see her, taking with him a daguerreotypist.

At that time, the circumference of the abdomen was seven feet six inches and the distance from the ensiform cartilage to the pubes was three feet six inches. The tumor of the buttock extended along the thigh, and measured two feet six inches in length and eighteen inches transversely.

There was some pustular eruption on the skin over the ischiatic tumor, but in general her health was good and her functions well performed. Menstruation was regular as to time and quantity, although painful during the last few years.

Towards the close of 1853 the cutaneous affection increased, her health failed, and she died January, 1854, at the age of thirty-six, and eleven years after the disease was first noticed.

An autopsy was not allowed, but, in order to get her into some sort of a coffin, the attending physician removed the posterior tumor in the presence of her husband. Within it was a cavity into which his arm could be passed to the elbow. He then passed his arm upward into the pelvis and abdomen, and, with the other hand upon the tumor externally, he satisfied himself that the abdominal and pelvic viscera were intact, and that the tumor was external to the peritoneal cavity. The cavity in the posterior tumor was a process of the peritoneum; the two tumors were portions of one and the same growth, and the point of egress was through the ischiosciatic notch.

The growth removed consisted mainly of a soft, adipose structure interspersed with delicate layers of fibrous tissue, in bulk enough to fill a common washtub, and the entire mass of both growths was estimated to be about 268 pounds.

The rate of growth is usually extremely rapid, although occasionally it is fairly slow. Sometimes a tumor grows slowly for a considerable length of time and then, without known reason, assumes remarkable activity of growth. Bigelow's tumor grew to the size of a coconut within three years, while MacEwen's tumor required nine years to attain the weight of three pounds. The growth is stimulated to remarkable activity during pregnancy, during which time it may attain very large size. The effect of menstruation upon the rate of growth has already been considered.

Degenerations.—Fibroid tumors of the vulva are said to be more likely to undergo degenerative processes than similar tumors in other parts of the body. Two factors are chiefly responsible: (1) the marked



FIG. 6.—EDEMATOUS FIBROMA (drawn from Harrington).

variations in the blood supply during menstruation and pregnancy; and (2) the fact that the tumor, when growing rapidly, soon becomes pedunculated, also often with circulatory disturbances.

Edema is most common (Fig. 6). The tumor's surfaces are also

very likely to suffer abrasions which, because of an unbalanced circulation, soon become ulcerated with resulting infection. Gangrene may result. Hyaline degeneration is very common as are cystic changes. Calcification is frequently observed and lymphangiectases have been described. Many of the tumors are classed as myxofibroma.

Most interesting, however, is the tendency to sarcomatous changes. Leonard, in his careful review, states that nearly one-fifth of the cases reviewed by him had undergone sarcomatous changes.

Symptoms.—Even the larger sessile fibroma of the vulva rarely produces symptoms of pain or pressure or causes inconvenience other than chafing of the enlarged labium, save during menstruation or pregnancy. Occasionally, itching is a prominent symptom. The fibroids which develop in the rectovaginal septum may cause constipation, and in a case reported by Villiers and Damoge, retention of urine was deemed to have resulted from pressure of the calcified fibroid of the vestibule on the urethra. The larger pedunculated fibroids cause symptoms from weight alone and may, from their size, interfere with locomotion. Coates reports a case in which coitus was practically impossible, and Albert records one which interfered with parturition. The changes during menstruation have been alluded to above. When a tumor becomes swollen and edematous, ulcerations are likely to follow, and in the event of secondary infection, which is usual, the growth becomes very sensitive. If the tumor undergoes malignant change, which is a frequent occurrence (one-fifth of the cases collected by Leonard), ulceration is the rule. Such tumors may be exquisitely sensitive.

Nonpedunculated tumors in the inguinal canal may give rise to pressure symptoms and in addition to producing a dragging sensation, may cause pains radiating down the thigh.

Diagnosis.—The diagnosis offers no difficulty, although the origin of the tumor may not always be determined until its removal. The fibroma developing in the extraperitoneal portion of the round ligament has led to the most frequent errors of diagnosis. Quite naturally they are likely to be mistaken for an inguinal hernia, as has been noted by Heidemann, von Recklinghausen, Verneuil, and others. The case reported by Doormann had worn a truss, until the size of the growth demanded surgical interference. These errors are not surprising, since a tumor in this region usually simulates an inguinal hernia. Moreover, tumors of the round ligament are sometimes associated with inguinal hernias, as is evidenced by the cases of Hecker, Hofmarkel, Landau and others. The tumor reported by Nebesky was actually reducible through the inguinal canal. In at least one case (Coates) the round, firm, elastic mass was mistaken for a testicle and the diagnosis was held to be hermaphroditism.

The differentiation from irreducible omental hernias, from hydro-

cele muliebrum and from glandular masses is often attended with difficulty. In Klemen's 7 cases, the correct diagnosis was made only three times before operation.

Treatment.—The treatment is surgical removal, necessary even in cases which are not giving symptoms, because of the likelihood of sarcomatous change. The fact that the tumors classed as sarcomata have appeared benign clinically (we have not found a case which presented metastases), in no way invalidates this statement.

The result of removal is usually good and there are few deaths recorded after operation. There are no recurrences after removal. Other tumors, however, may subsequently appear in the same region just as new fibroids may form after myomectomy. There are a number of such cases in the literature, chiefly subperitoneal connective tissue or extraperitoneal round ligament fibroids.

LIPOMA OF THE VULVA

Lipoma of the vulva is rarely met with. This seems surprising, because lipoma in general is so common. The infrequency of these cases is well shown by the fact that no operator has yet recorded more than a single case in his own experience. Kelly, in 1903, collected 19 cases from the literature and added a case of his own. Since then, some 8 or 10 cases only have been recorded, of which we cite the cases of Hill, Fenno, Hutchinson, Olivieri, Carmalt and Sturmdorff. Prior to Kelly's paper, no author had collected more than 3 or 4 cases.

This class of tumors is worthy of consideration chiefly because they may attain considerable size. Degenerations of clinical importance are not common. The tumors do not appear to undergo malignant change. We know little as to the etiology save that they occur usually during the child-bearing age.

Location and Appearance.—Lipoma in this region occur either on the labium majus, or the mons veneris, and present the same characteristics as lipoma elsewhere. They are usually soft, but may be firm, since their feel depends upon the relative proportions of fat and connective tissue in the growth. The fat may be encapsulated, yet is more usually diffuse.

The tumors may be contained in the enlarged labia or mons, or may project from it by a large base. Later in their growth, they may sink down by their weight, drawing the skin out in the form of a pedicle. Rarely they grow up toward the inguinal canal and simulate a hernia, as in the case of de Smet (Fig. 7).

The skin surmounting the tumor usually appears normal, yet may be tightly drawn over it, or may be wrinkled or even lobulated. As a

result of friction, it may thicken or sometimes ulcerate. Occasionally the surface of the growth is covered by tortuous telangiectasis. The blood vessels in the skin are usually enlarged and may occasion severe hemorrhage if ulceration is extensive, as well as in the rare cases in which the patients attempt removal. Koch reports such a case which came to his attention because of the very severe hemorrhage which followed the woman's attempt to cut off the growth with a razor. In the same manner, Deekens records his case which had lost a quart of blood from the ulceration two weeks before operation.

Growth.—The rate of growth is usually slow, in marked contrast to fibroids of the vulva. Deekens' case, a woman of sixty-one, had carried the slow-growing tumor for seventeen years before ulceration

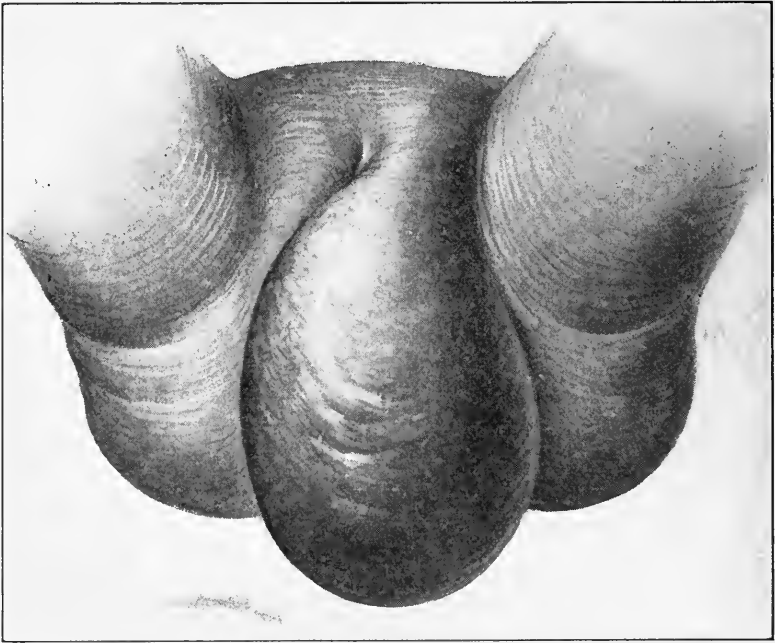


FIG. 7.—LIPOMA OF LEFT LABIUM SIMULATING A HERNIA (drawn from Goodell).

and the ensuing hemorrhage forced her to seek treatment. There are numerous cases in which the growth was carried ten years. The statement made in numerous texts, that the tumor grows rapidly during menstruation and pregnancy, is not substantiated by our review of cases, in which the very great majority were found in women during the child-bearing period.

Yet the tumor may attain considerable size. Balls-Headley's case is the largest, weighing twenty-four pounds: a number of other cases have weighed ten pounds, although the usual size is the "size of a fist."

Symptoms.—The symptoms depend largely upon the size and position of the growth. Smaller tumors may cause no symptoms, or at worst, only symptoms from friction. The larger tumors may occasion dragging sensations from the weight of the growth, and interference with locomotion. Several complained of difficulty in coitus. Bountzel's case was the size of a fist for four years, enlarged during labor to the size of a child's head and retarded labor. Sturmdorff's case also partially blocked labor (together with an old ankylosis of the right hip).

Diagnosis.—The diagnosis may be confusing. The soft tumors may be readily mistaken for cysts. Goodell's case was explored for fluid with the needle without result before the diagnosis was made. Many others gave a sense of false fluctuation, notably de Smet's, and Henningsen's. The growth may be confused with a hernia. Balls-Headley's case was not only fluctuant, but the impulse on coughing was conveyed to the labial growth weighing 24 pounds. Lipoma has also been confused with elephantiasis, cysts, adrenal rests (Andrews) and fibroma.

Treatment.—The growth can be removed without difficulty, shell-ing out the entire fatty capsule. After all bleeding points are ligated, raw surfaces should be approximated and the incision should be united with horsehair sutures.

SWEAT GLAND TUMORS OF THE VULVA

Sweat gland tumors of the vulva have been found so seldom that they may be counted as among the very rare neoplasms of this structure. There are only some 20 cases which have been described, although the growth is usually so small, and causes symptoms so rarely, that it is quite likely that it occurs far more frequently than these figures suggest.

Braun, in 1892, described the first case of which we have record in which the diagnosis was correctly made, yet his observation created little interest, and it was not until Pick, in 1904, presented his study that the attention of pathologists was directed to this rare tumor. Nearly all the cases reported have been observed in Europe. Thus far only the cases of Outerbridge and Schwarz have been reported from America.

Classification.—L. Pick, in 1904, after a careful and painstaking study of his 2 cases, and a review of the few cases then present in the literature, concluded that we should distinguish carefully between the tumors which presented indisputable points of origin from the vulvar sweat glands (*hidradenoma tubulare*) from those in which the origin

could not be definitely proven (adenoma hidradenoid), even though both types of tumor presented certain similar histologic features.

The hidradenoma tubulare, as the name implies, is an adenomatous structure containing acini lined with a double layer of cells which are supported by elastic tissue, the whole mass being inclosed by a definite membrana limitans of elastic tissue. A sudoriferous duct originating in the adenoma can be traced to its opening in the skin.

Adenoma hidradenoid presents rather similar histology, yet proof of its origin from completely developed sweat glands is lacking in that

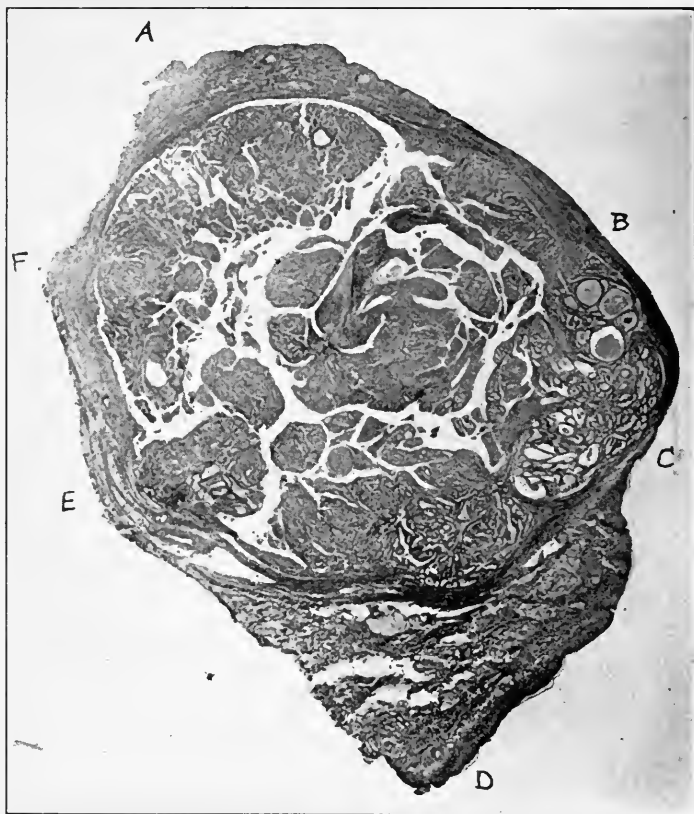


FIG. 8.—SWEAT GLAND TUMOR OF VULVA. Low power photograph of section through entire tumor and surrounding tissues (Outerbridge).

there is no sudoriferous duct, nor connection with other sweat glands. Some, as Landsteiner and Outerbridge, have objected to this classification on the ground that it is complicated and suggest the term "hidradenoma" to designate all adenomatous tumors presenting a histologic picture suggesting sweat glands. Practically all the cases in the literature, however, are reported on the terms of Pick's classification.

There is no essential difference between the solid and cystic type

of cases, since the latter arise from the former by accumulation of the secretion of the glandlike tumor.

Etiology.—Little is known of the etiology, besides the fact that these tumors originate in vulvar sweat glands. The cases presenting for treatment have all been older than thirty-five, although many of the growths were first noted in the twenties.

Histology.—The hidradenomata are usually situated in the corium, and are composed of adenomatous or papillary structures containing innumerable irregular acini and tubules, separated by exceedingly delicate connective tissue septa. The acini are lined in many places by a double layer of nonciliated cells, an inner layer of high cylindrical

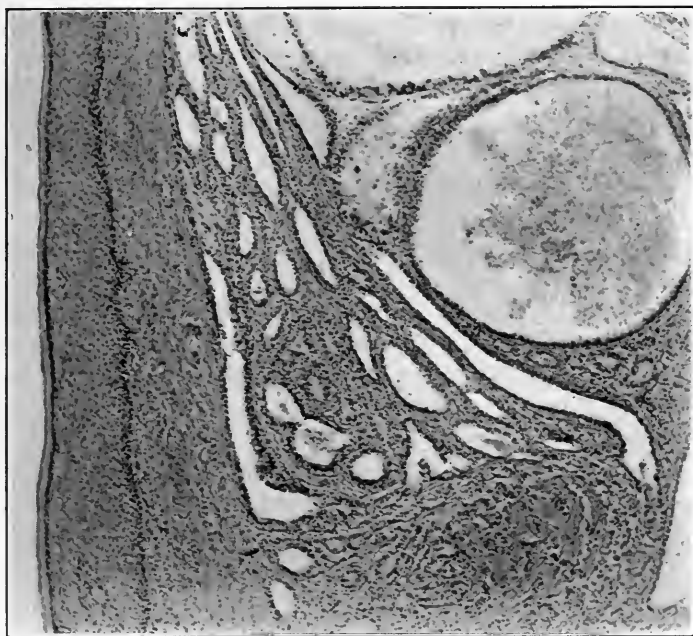


FIG. 9.—SWEAT GLAND TUMOR OF VULVA. High power, through areas at *b*, Fig. 8, showing cystic acini and squamous epithelium of epidermis.

cells surmounting a layer of shorter and more irregularly shaped cells. Each acinus is surrounded by a definite layer of elastic tissue. In some places, the superficial squamous epithelium of the labium sends down long prolongations which communicate with the acini of the tumor. The tumor is usually well limited within its bounding membrane of elastic fiber, yet the cases of H. Ruge, Outerbridge (Figs. 8, 9) and Schwarz have presented areas of its invasion.

Size, Appearance and Location.—The growth is usually of small size, frequently described as “pea size,” or “cherry stone size,” and only Schroeder’s case was as large as a walnut. It usually presents as a subcutaneous circumscribed neoplasm which may be either firm or

cystic, although it has been described as a broad, pedicled, mushroom-shaped tumor (case of Pick). It is covered with skin which may be ulcerated from the trauma of continued friction. The tumor is usually single. It may be multiple, as shown by one of Pick's cases, which had three tumors, and the case of Gross, which had four. The growth may appear in any part of the labium majus or minus; it has been found as high up as the urethral orifice, and as low down as the posterior commissure.

Usually imbedded in the vulva, it presents no definite color. Williamson's case, however, was definitely pink, probably from secondary disturbances of circulation, since the growth was ulcerated and bled very readily when touched.

The rate of growth is usually very slow. Many of the tumors had been known to have been present for ten years. Schroeder's case had had a small cyst for ten years, which had not grown noticeably until a few weeks before coming for treatment.

Symptoms.—The growth is usually so small that it does not cause symptoms, unless it has begun to grow rapidly, or has become ulcerated and infected.

Question of Malignancy.—The tumors are accounted benign, although some question as to the frequency of malignant changes or features has been raised by the cases of H. Ruge, Outerbridge, and Schwarz. Ruge considered that his case had become carcinomatous, although all who have reviewed his work do not agree with him. Outerbridge and Schwarz viewed their cases rather with suspicion, since the former found acini which had invaded the stroma, while the latter found an extension of solid masses of round or polyhedral cells into the same structure.

Diagnosis.—The diagnosis may be suspected on finding a small, firm tumor in the labia attached to the under surface of the skin. The final diagnosis can be made only with the microscope.

Clinically, sweat gland tumors may be confounded with small sebaceous cysts, with cysts originating from aberrant urethral ducts, with labial cysts lined with ciliated epithelium and probably of embryonal origin, with cysts of the wolffian ducts, and with chronic inflammatory conditions of Bartholin glands.

Treatment.—The proper treatment is removal, since the number of cases which have been studied is too few to warrant the belief that the tumor may not develop malignant tendencies.

CYSTS OF THE HYMEN

Cysts of the hymen are very rare. Gellhorn, in his careful review of the literature up to 1904, could find but 17 cases, most of which were noted in the newborn. Rarely they occur in youth. They are located

most frequently on the outer surface of the hymen and generally are very small. They may attain the size of a cherry. Most of the reported cases are single growths. The case reported by Ulesko-Stroganowa had a small cyst on each side of the hymen. Ricci's case had a small tumor included in the wall of a larger one. One of Ziegenspeck's cases had two small cysts at the base of the main cyst. Piering observed a case in which the margin of the hymen was surrounded by a number of small transparent cysts.

Microscopic Appearance.—The covering is squamous epithelium derived from that of the hymen. The stroma wall is composed of more or less dense connective tissue arranged in layers, sometimes thrown into well-developed papillae. Numerous capillaries are present, occasionally in masses of smooth muscle fibers. The inner surface of the cyst wall is lined with epithelium which may be of the cuboidal type, although it is more often of the pavement variety. Marchesi's case was lined with high cylindrical epithelium.

Histology.—The cysts may contain a watery fluid or a homogeneous jellylike substance of yellowish brown color or a mass of epithelial detritus. Blood corpuscles were noted by Ulesko-Stroganowa. Ricci's cyst was composed of detritus of blood corpuscles, fat droplets, epithelial cells in large numbers suspended in the dark brown liquid.

Etiology.—Various theories have been given to account for the origin of cysts. Ricci has stated that they may arise from embryonal epiblastic remnants contained within the stroma. Bastelberger advanced the view that they resulted from invagination and separation of the epithelium of the hymen. Döderlein's view was rather similar in that he thought they resulted from the coalescence of folds of the hymen. One of Gellhorn's cases rather supports the last view, since fibrous bands were found extending out into the hymen and separating a mass of epithelium. Some regard them as retention cysts. Piering thought that they might arise from distended lymph spaces. Others hold that they develop from the glands which are occasionally found in the hymen. Ulesko-Stroganowa and Marchesi thought that their cases arose from wolffian ducts, since they were lined with cylindrical epithelium. Palm attributed his case to a dilatation of sebaceous glands.

Symptoms.—Symptoms depend upon the size of the tumor. Usually the growth is small and is discovered accidentally.

Treatment.—The treatment is excision.

Other benign neoplasms of the hymen are very rarely noted. Polypoid tumors and angioma have been described.

OTHER BENIGN TUMORS OF THE VULVA

The majority of these are only pathological curiosities and are extremely rare.

There are few cases of neuroma of the vulva in the literature. Simpson reports one in which the tumor was a painful nodule situated in the labia near the urinary meatus. Kennedy reports a case in which the tumor presented as extremely tender tubercles.

Teliangiectatic angioma, chondroma, and cysts have rarely been encountered.

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CHAPTER II

MALIGNANT TUMORS OF OUTLET

Carcinoma of vulva—Frequency—Age—Etiology—Appearance and structure—Classification—Extension—Symptoms—Diagnosis—Prognosis—Treatment—Results—Carcinoma of the clitoris—Type of growth—Frequency—Etiology—Age—Location—Appearance and form—Histology—Symptoms—Treatment—Carcinoma of Bartholin glands—Classification—Etiology—Age—Gross appearance—Symptoms—Diagnosis—Prognosis—Treatment—Literature—Sarcoma of the vulva—Classification—Frequency—Etiology—Age—Point of origin—Location and appearance of growth—Metastasis—Clinical picture—Symptoms—Diagnosis—Treatment—Prognosis—Literature.

CARCINOMA OF THE VULVA

This condition attracts attention because of its extreme malignancy. There are some, as Dittrick, who have made fairly extensive reviews of the literature without finding record of a single five-year cure.

Frequency.—Vulvar carcinoma is a rare disease in comparison with carcinoma in other parts of the generative tract. When we consider the inevitable trauma associated with child-bearing, etc., it seems as if these tissues possess an increased resistance to malignant changes.

The frequency of carcinoma of the vulva is variously stated, although all emphasize its rarity. Rothschild, in 1912, was able to collect but 395 cases. Ederle, in 1919, found that the series reviewed by Gurlt, Schultze, Engström, Teller, Frankl, Lutzenberger, Ossing, and Rothschild total 677 cases. Flater found but 8 cases in 6,407 gynecologic patients in the University Frauenklinik of Heidelberg from 1902 to 1909. Rothschild states that there were only 6 cases in 9,643 gynecologic patients in the Freiburg University Frauenklinik during the years 1904 to 1911. Combining the comprehensive statistics of L. Mayer, Gurlt, Winckel, Gönner, Schwarz, Eisenhart, Blümcke, Tipjakoff, Lipinski, and de Leon, Björkvist found that vulvar carcinoma occurred once to 821 gynecologic patients (0.12 per cent).

The relative frequency of carcinoma of the vulva and carcinoma of the uterus, including in the latter the cancers of both the cervix and the uterine body, varies considerably with different observers. Virchow gives it as 1 to 40; Gurlt, as 1 to 48; Schwarz, as 1 to 38; Burghelle, as 1 to 35 or 40; Frankl, as 1 to 29; and Flater, as 1 to 27. The percentage which carcinoma of the vulva constitutes of carcinoma of the female genital tract varies considerably. Von Winckel, basing

his observations on 1,068 polyclinic cases, found 0.6 per cent; Gurlt, 1 per cent; Pissemksz, 1.7 per cent; Schottlaender, 2.1 per cent; Savare, 4 per cent of 300 pelvic carcinoma; and Gönner, 5 per cent of 99 cases. We have seen 7 cases in a series of 140 pelvic cancers.

Jacoby itemizes the incidence of 355 pelvic cancers in women as follows:

Pelvic Cancer	Cases	Per Cent
Of uterus.....	317	89.3
Of ovary.....	23	6.5
Of vagina.....	10	2.8
Of vulva.....	5	1.4

Age.—Carcinoma of the vulva is most often seen in old age. Rothschild, in 1912, analyzed 395 cases of carcinoma of the vulva which he collected from the literature and found that more occurred between 60 and 70 years than in any other decade. Winckel found the greatest frequency in the sixth decade. This agrees with the findings of Kehrer, Eberhart, West, Dittrick, Winckelmann, and Frankl. A smaller group have found the greatest frequency in the fifth decade. Dittrick states that 84 per cent of the cases which he collected from the literature were more than 45 years of age. The cancer, however, does occur at an earlier period, and has been noted in childhood. Krysiewicz noted a case at 4 years. St. Germain, Launois, le Fileux, each described cases at 5 years, although there is some dispute in all 4 cases as to whether the tumor was sarcoma or carcinoma. Kinoshita recorded a case 14 years old; Mertz, 16 years; Lambert, and Fritsch, each a case 18 years, Albert, 20 years; Engström, 21 years; Berecz, 23 years; Townsend, 24 years; Perruchet, and Lutzenberger, each a case 25 years.

Etiology.—The etiology is not known. Various factors have been adduced as predisposing causes. Rothschild voices the feeling of nearly all students of the question when stating that labor, or operative trauma associated with labor, does not seem to be an etiologic factor. This is substantiated by the fact that the disease often occurs in nullipara or virgins. Lutzenberger found that 11 of 106 vulvar cancers occurred in nullipara or virgins. However, Aschenborn reported one case in which the tumor seemed to begin shortly after confinement and another case occurring in a woman who had had eleven forceps deliveries.

Nearly all admit that trauma may be of very great importance as a predisposing factor. West, Ingeman and Amitin, Aschenborn, and Taussig have reported cases, the development of which seemed closely related to a fall in which the vulva was bruised. Many others have reported cases which developed in the site of a wound which remained unhealed for a long time.

Pruritus appears to be most important as a predisposing factor, and many men have emphasized the fact. Pruritus is a symptom which may be the result of many conditions, such as senile changes of the labia and vagina, irritation from leukorrhea, the urine of diabetes, uncleanliness, masturbation, etc. Tasty, and also Sassy, go so far as to claim that pruritus is the sole predisposing cause. Some, as Basset, while recognizing that pruritus is a constant initial symptom, differentiate between the various conditions which are responsible for it.

A voluminous literature also emphasizes the association between leukoplakia and kraurosis as forerunners of vulvar carcinoma. The importance of leukoplakia as a forerunner of cancer was emphasized by Reclus and Besc in 1887. Becker, Bochinski, Brettauer, Jacobs, Yaile and Bender, Martin, Schwarz, Teuffel, and a number of others have described cases of vulvar carcinoma which developed in kraurotic labia. Yaile and Bender describe 14 cases and Butlin 3 cases in which the disease arose in leukoplakic patches. All, however, do not agree. Frankl states that, in the many cases which he saw in the Schauta clinic, there was only 1 during six years in which there was present leukoplakia and carcinoma.

Carcinomatous degeneration of benign tumors of the vulva have been described by Cohnheim and a long list of others. Benign tumors of the vulva are not uncommonly noted. Cohnheim thought that the little papilloma often preceded the malignant tumor. The disease followed luetic ulcers in the cases of Arnot and Hutchinson. Maurel described a case following psoriasis. Taussig, who saw 2 cases in young women having artificial surgical menopause, re-advanced the older suggestion that ovarian secretion may inhibit the development of the tumor, especially since 80 per cent of vulvar carcinoma occur in women past the menopause.

Appearance and Structure of Growth.—The tumor may arise from the squamous epithelium of the labia minora or majora (carcinoma of the clitoris is included in a separate chapter). In the beginning, the growth appears either as a small, warty tumor or as a localized thickening or ulcer (Fig. 11). At the site of the lesion, the skin is excoriated and pigmented as a result of scratching. At first, the discrete nodule or plaque is freely movable over the underlying tissue. Ulceration usually occurs early (average of six months) and, shortly following, the growth becomes fixed to the deeper tissues. The tumor then begins to grow rapidly and may assume either a vegetating fungoid type or the infiltrating form (Maurel). On section, the tumor appears as a white, pearly mass in which are yellow spots of necrosis. With the growth of the tumor, the epithelial cords dip down into the underlying tissues and gradually involve them. Finally, the bones are invaded. The infiltrated form does not elevate the overlying skin. It ulcerates early and infiltrates the surrounding structures. The edges of the early ulcer

are elevated and undetermined. Later, the typical craterlike form is seen.

Classification.—Histologically, the growth has been divided into four types: (*a*) scirrhus; (*b*) medullary, depending upon the amount of connective tissues; (*c*) cancrioid, characterized by numerous epithelial

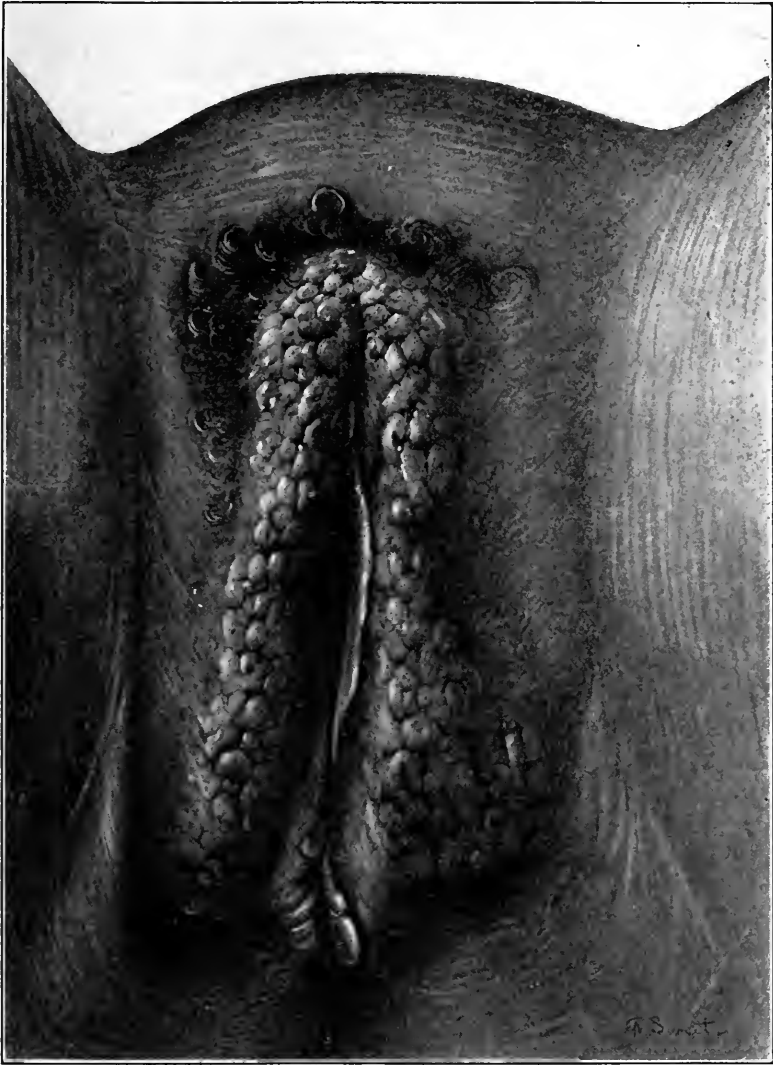


FIG. 10.—SYPHYLOMA OF VULVA RESEMBLING CARCINOMA.

pearls; and (*d*) melanocarcinoma, presenting numerous brown or black pigment granules, in or between the carcinoma cells. Several observers agree with Rothschild in believing that the tumors of this latter type, which have been reported for the most part in earlier literature, were really sarcomata.

Method of Extension.—The tumor spreads chiefly by the lymphatics to the neighboring lymph glands which it soon involves. More rarely, it grows by contact, although there are many cases which illustrate the possibility. The growth early extends into the lymph spaces and causes degenerations of the adjoining tissues. The inguinal lymph glands, both superficial and deep, are early involved and, later, the iliac, sacral, lumbar, and abdominal glands are invaded. The pelvic glands may be involved secondarily to the inguinal nodes or primarily through extensions through the lymphatics of the vagina. The inguinal glands may attain such large size as to interfere with the blood supply of the leg and cause edema and even gangrene. Metastatic nodules may develop in tissues on the opposite side of the labia. The disease may become widely disseminated and may involve the lung, liver, heart, spleen, kidneys (Kuestner, Leger); pleura, lungs, heart, (Arnot); or axillary glands and breast (Zeiss).

Symptoms.—The tumor may be present for some time without causing symptoms, although usually pruritus is a marked complaint. This symptom may come on in paroxysms and may cause itching, burning, or pricking sensations. It is often present in the stage in which the tumor is not defined and when a definite diagnosis cannot be made. The importance of this symptom in women at or beyond the menopause cannot be too strongly emphasized. Patients presenting this complaint should be examined carefully and frequently because so few vulvar cancers are really cured.

Pain is usually a late symptom and comes on with the ulceration. Later, there is a discharge of a whitish, mucoid character which soon becomes bloodstained. Hemorrhage is usually a terminal event. Urinary symptoms of burning, scalding, or incontinence, result when the urethra has become involved by either primary or secondary extension. Death may result from cachexia, chronic sepsis, infection of the urinary tract, or emboli.

Diagnosis.—The diagnosis is usually easy from the signs previously described. The condition must be differentiated from lupus, sarcoma, and luetic ulcers. The former usually comes on in younger women, leads to dense scar formation, and tends to heal under treatment. Sarcoma is very rare and can be differentiated only by microscopic study. Syphiloma may cause some difficulty but the history, Wassermann reaction, and the therapeutic tests, should establish the diagnosis (Fig. 10).

Prognosis.—The prognosis is extremely grave. Death invariably results unless the entire tumor is removed. The duration of the disease varies considerably, from a few months to several years, although there are no cases reported in the literature in which the course of the disease was not influenced by some type of treatment (often one which aggravated the condition).

Treatment.—The treatment of carcinoma of the vulva, clitoris, and Bartholin glands is identical with that of any malignant condition in this area. At present, the only hope of cure is a surgical removal of the entire growth by a wide dissection, not only of the local parts but of the lymphatics which drain the area. Operation is extremely difficult because of the anatomy of the lymphatic channels. The vulvar tissues are well supplied with lymph tracts which drain in different areas. The prepuce and labia drain into the inguinal glands. The glans clitoris



FIG. 11.—CARCINOMA OF RIGHT LABIUM MINORA IN WOMAN OF SEVENTY.

empty chiefly into the crural and inguinal glands which anastomose with the pelvic nodes. Cross drainage to the other side is present.

Theoretically, the operation should include in one piece the removal of the entire labia and clitoris, together with the external inguinal glands and the structures which lie between the glands and the tumor (Fig. 12). More should not be attempted, since, if the disease has invaded the pelvic glands, the condition cannot be cured by any procedure now known. The literature contains descriptions of many more extensive methods which have been tried, unsuccessfully for the most

part, upon women in whom there was widespread local involvement and apparent invasion of the glands. The same rules should govern the treatment of malignant tumors of the vulva as have been developed for cervical cancer, that is, to treat by surgery only the cases in which there is every reason to believe that operation will cure.

The fact that many have claimed that there is no improvement in the operative result from removal of the glands indicates probably that their cases were extremely late. On the contrary, Hoffman reports a case in which recurrence was noted after a radical operation only after eight years. This was operated again, and two years later

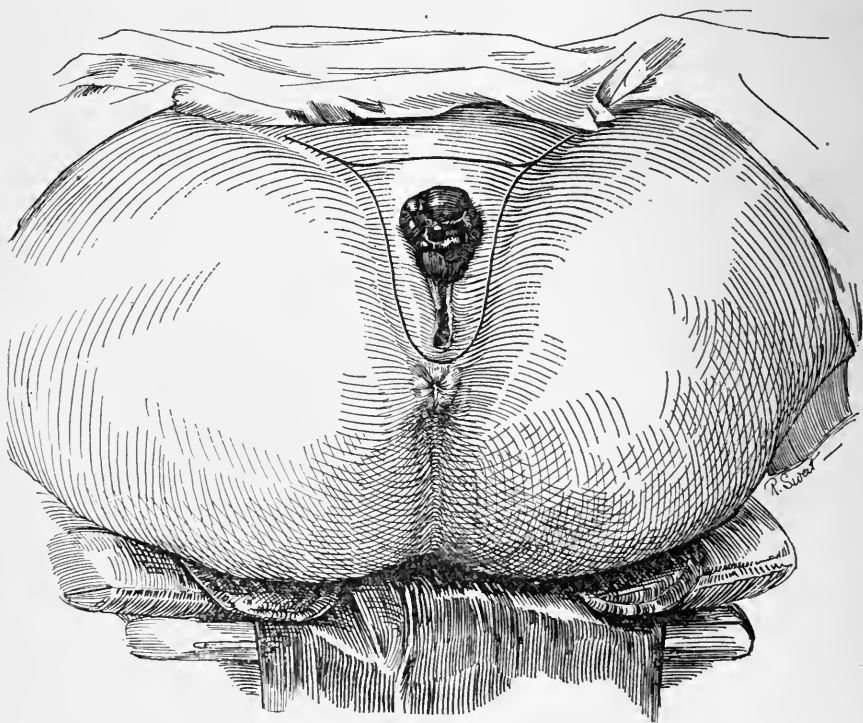


FIG. 12.—AREA OF REMOVAL FOR CARCINOMA OF VULVA.

another recurrence developed, also operated, a third recurrence two years later, and again after three years, and a final recurrence after two years. All these recurrences were operated, the woman living at least seventeen years. Lewers operated four times in five years on another vulvar cancer. The first operation removed the tumor and the right-sided inguinal glands: the second time for a local recurrence; the third time because the incision had not healed, at which time he removed the left inguinal glands; the fourth time there was a local recurrence. Five years after the last operation, there was no sign of recurrence and the woman was free from pain. Both of these cases presented fairly early growths.

There is some discussion as to whether the operation should be performed with the thermal cautery or the knife. Both methods have their advocates. All agree that, if the knife is used, great precautions are necessary to prevent wound implantation. The tumor should be surrounded with gauze and touched only with forceps. The undeniable advantage of operation with the knife is union per primum.

Stoeckel, McCann, Maclair, and Basset have described operative procedures which permit the removal of the entire mass in one piece. The tumor is removed from above in all cases.

Stoeckel makes an incision on the abdomen at the outer border of the rectus muscle down and along Poupart's ligament over the mons veneris and up and out in the same manner on the opposite side. This incision would permit an extraperitoneal removal of the iliac glands were such a procedure contemplated. After the inguinal glands are removed on each side, the tumor is dissected, together with the labia, working down from above.

McCann made an incision parallel to Poupart's ligament on each side, beginning at the iliac spines. The inguinal and crural glands are removed with the surrounding fatty tissue, together with the tumor. He also attempted the extraperitoneal removal of the iliac glands.

Maclair ligated the external iliac artery and removed in succession the crural glands, those of the femoral canal, the inguinal and finally the iliac glands, after which the tumor was excised. This operation has few advocates.

Basset developed a procedure on the cadaver which permitted extensive removals by a fairly conservative procedure. The skin incision runs from opposite the anterior superior iliac spine, downward and inward to the femoral canal and then, from the same point, downward and inward to the external inguinal ring, stopping at the level of the pubic tubercle.

The fascia of the external oblique is cleansed and split parallel to the inguinal canal in its whole length. The round ligament appears. The internal oblique and transversalis fascia are separated from Poupart's ligament which bares the entire length of the round ligament. By retracting upward, keeping outside of the round ligament, the lateral retrocrural glands appear and are removed. They lie in the region of the origin of the deep circumflex iliac artery.

He then divides Poupart's ligament just inside the femoral vein, ligates and divides the inferior epigastric vessels which gives exposure of the median retrocrural glands. Cloquet's gland lies near the femoral veins in the pectineal fascia. It is removed. By downward retraction, the cellular and fatty tissues are now removed from the margins of Scarpa's triangle down to the labia majora. The deep femoral glands lie along the femoral vein.

He advises closure of the first incisions before attempting the

removal of the tumor. The edges of Poupart's ligament and the pectineal aponeurosis are united to the ligament corpori, without compromising the femoral vein. The muscles are then united to the reconstructed Poupart's ligament just as in a hernia. The tumor is then removed.

Roentgen rays have been tried by many surgeons without good results. They have not seemed to be of much value as a post-operative procedure.

Radium has been used often in comparatively recent times. We have tried it in several cases without good results, yet all the cases were late and presented well-developed inguinal tumors. Bumm, in 1913, treated one operable vulvar carcinoma with radium and reports a five-year cure. In 1914, he treated 7 operable cases with four-year cures in three. In 1915, he treated five operable tumors with recurrence following in all cases three years later.

Results.—The results are not good. Dittrick reviewed the literature without finding a single case which he felt should be considered as a five-year cure. Goldschmidt tabulated 214 cases studied from a period from five to eight years and found 8 cases which did not give evidence of recurrence. Kuestner, Zweifel, Grünbaum, Teller, and Keeling report cases which recurred after eight to twelve years. Rothschild found that 51 of his 225 collected cases had been lost for the purposes of study. Death resulted from intercurrent affections or from a cause not stated in 10 cases. Of the 164 cases which remained, recurrence was observed in 142, or 82 per cent. Recurrence presented in 47 per cent of these during the first year. Many of these cases (34) had the glandular returns removed shortly after their appearance. Of the total number, 4.87 per cent were free from recurrence at the end of five years. The disease returned in 8 of the 164 cases in periods of from five to ten years. Recurrence was observed in the glands three times more frequently than in the region of the primary tumor.

CARCINOMA OF THE CLITORIS

At first glance, it does not appear that carcinoma of the clitoris deserves consideration apart from that of the vulva. The clitoris merely forms part of the vulva. Its tumors present problems identical with those of the vulva in general. Yet we know so little of cancers in general that we should not fail to take advantage of every bit of work that has been done in a careful and critical manner.

Since the first case of carcinoma of the clitoris was reported by Hutchinson in 1850, there has accumulated a considerable literature. Douriac, in 1888, made the first extensive review and collected 22 cases, Björkvist, in 1903, cited 65 cases. Jacoby, in 1904, tabulated 67. Basset, in 1912, collected 147 and worked out details of treatment. By

1919, the number of reported cases had grown to such an extent that Ederle was able to collect 183 which formed the basis for his critical review.

Type of Growth.—Epithelioma arising from the squamous cell epithelium is the usual type. A few adenocarcinoma have been described. The tumors may be primary, or secondary from carcinoma in adjoining parts of the labia.

Frequency.—Various attempts have been made to show the frequency. In the cases of Gurlt, Schultze, Engström, Teller, A. Frank!, Lutzenberger, Ossing, and Rothschild, there were 677 vulvar carcinoma, 109 of which were in the clitoris (16 per cent).

Etiology.—The etiology is not known. Nearly every possible theory has been advanced, but none seems applicable to any considerable number of cases.

A small number of instances in which the disease occurred in the young may be explained possibly by the Cohnheim theory. Some form of chronic irritation has been urged as the causal factor of the larger group of cases, yet the relation is rarely conclusive.

The idea that excessive sexual activity or masturbation, etc., may have much to do with causing the disease seems disproved by the fact that very few of the cases occurred in prostitutes, and on the contrary a very appreciable percentage were observed in virgins. Rather closely related is the theory that the growth is likely to follow chronic inflammatory processes, and especially those which led to pruritus. Cumston and Hutchinson thought that syphilis was a factor. The same objections apply to both. Pruritus and syphilis unfortunately are very common, whereas carcinoma of the clitoris is extremely rare.

More tangible is the view that there is a definite relationship between leukoplakia, kraurosis and carcinoma of the clitoris. This is confirmed by the findings, yet there is a tremendous percentage of these cancers that have never had either leukoplakia or kraurosis. The association of leukoplakia and carcinoma of the clitoris is proved by 7 cases. Six cases developed in kraurotic areas, and 2 cases in the literature had had both leukoplakia and kraurosis.

Many have called attention to the fact that benign tumors are more likely to undergo carcinomatous changes in some areas than in others. We have already noted the high proportion of sarcomatous changes in vulvar fibroids. Nonmalignant tumors of the clitoris are not common, yet there are 8 cases in the literature in which benign tumors, such as papilloma, fibroma, angioma and cysts of the clitoris, were followed by carcinoma.

It is more difficult to establish a relation between actual trauma and carcinoma of the clitoris. There are, however, three cases in which the disease followed trauma not associated with childbirth. One of these was injured while sliding on an icy hillside and another in a fall.

Attempts to associate the disease with lacerations of the clitoris during childbirth or from forceps injuries have failed.

Parity.—While the disease is practically one of women who have borne children, it has occurred in a considerable number of nullipara and a definite percentage of virgins.

The parity in 66 cases is given as follows:

0- 1 para	19 cases
2- 4 para	16 cases
5- 7 para	12 cases
8-10 para	14 cases
11-13 para	5 cases

Menopause.—The older authors believed that the disease was more common about the menopause. This view no longer holds.

Age.—The age incidence is practically that of vulvar carcinoma, though there is a larger proportion of cases in the young. There is a rapid increase in the number of cases after the age of 40. The greatest incidence is in the seventh decade as shown by Ederle.

EDERLE'S TABLE

Years	Cases	Per Cent
20-30	7	4.4
30-40	11	6.9
40-50	23	14.5
50-60	40	25.1
60-70	61	38.4
70-80	15	9.4
80-90	2	1.3

Location.—In the majority of cases, the tumor is situated in the folds of the nymphæ, between the large and small labia; more seldom in the glans; least often in the prepuce of the clitoris.

Gross appearance and form.—Three types of primary tumors have been described: (1) a more or less circumscribed growth (Fig. 13); (2) one presenting as a diffuse infiltration; and (3) a form suggesting Paget's disease, in which the growth does not give the usual picture of malignancy.

(1) The growth is more or less circumscribed. Under this heading are three subtypes:

- (a) One in which there is an ulcerated tumor sharply demarcated from the surrounding tissue.
- (b) A papillomatous tumor frequently with a definite pedicle.
- (c) Enlargement of the clitoris yet preserving more or less of its normal outlines.

(2) The growth presents as a diffuse infiltration which is firmly fixed to the deeper tissues. Occasionally the skin surmounting the growth is



FIG. 13.—CARCINOMA CLITORIS WITH AREA OF IMPLANTATION BY CONTACT ON THE LEFT LABIUM MAJUS (Kelly, Operative Gynecology).

elevated *en masse*. It may, however, show only small islands of elevation.

(3) A form somewhat resembling Paget's disease. The skin in this type is soft, but contains scattered through it at intervals a num-

ber of small pea- to bean-sized nodules. At the edge of the neoplasm is a fine, white, slightly raised epithelial border. This type at first sight does not suggest a cancer. The diagnosis usually is made only with the microscope.

Cancers of the clitoris which develop secondary to carcinoma elsewhere are frequently described. Most of these are direct extensions from carcinoma of the labia. Yet there are a number of cases recorded in which the clitoris was finally involved by direct extensions from carcinoma of the uterus, which sent off offshoots through the vagina until finally they reached the clitoris. The clitoris may also be the seat of metastases from cancer of the uterus, and 7 cases of this complication have been described. Weibel reports a case in which the metastasis appeared subsequent to the operative removal of the uterus. Some men have tried to prove that carcinoma of the ovary has given rise to metastases in the clitoris. Such cases, however, are difficult to establish.

Histology.—There are two types of squamous cell carcinoma of the clitoris; the infiltrating, cornifying epithelioma, and the flat, ulcerating, basal cell type. The former is more common.

Adenocarcinoma have also been described (Bertino), arising as primary growths from the epithelium of the sebaceous or sweat glands of the prepuce of the clitoris, or a secondary metastasis from other adenocarcinoma of the pelvis.

Symptoms.—Itching, as in other carcinoma of the vulva, is usually the first symptom. After a longer or shorter period, sticking pains appear first in the vulva, then in the inguinal regions and later in the extremities. With the advent of ulceration, there is a serosanguineous discharge which soon becomes foul, and which may lead to excoriations of the thigh which do not heal readily. Bleeding is a late symptom and usually is present only when the growth is sloughing. This seems rather remarkable, because the clitoris is such a vascular organ. Dyspareunia is common. Urinary symptoms are usually present. At first merely tenesmus, there may follow obstruction to the flow when the meatus becomes involved. Later there is incontinence. Walking is painful, especially in the later stages because of the excoriations on the thighs and the ulceration of the labia. Pressure symptoms may result when the inguinal glands attain size sufficient to exert pressure on the nerves or to cause mechanical interference with the circulation.

Treatment.—The treatment is similar to that of vulvar carcinoma (q. v.).

CARCINOMA OF BARTHOLIN GLANDS

Carcinoma developing primarily in Bartholin glands has very rarely been described. The largest series of which we find record is Spencer's,

who, in 1913, in London collected 18 cases. There are a number of other cases scattered through the literature, but the list is not large. Until 1915, there were only 15 cases in the German literature. In this country, Kelly reports a single case, as has Peterson, and a few others. We have met with only 1 case in a fairly large series of pelvic cancers. Quite possibly the condition occurs more commonly than is indicated by the literature, since in vulvar carcinomata which come late for treatment it is often quite impossible to ascertain the point of origin of the growths.

Classification.—The chief interest attached to cancers of the Bartholin glands, other than those of the vulva in general, lies in the fact that both squamous cell carcinoma and adenocarcinoma have been proved to develop in the Bartholin glands. Since this at first sight seems incredible, it is worthy of consideration. Both types occur with equal frequency.

The acini of Bartholin glands are lined with columnar epithelium. Consequently a cancer developing in this lining will be an adenocarcinoma. Observers are not agreed, however, as to the character of the cells lining the gland ducts, other than that they are of the transitional type. The chief ducts usually show a layer, two, three or four cells deep in the mid-portions. Near the point at which it opens on the vulvar skin, the lining passes over to the skin type of squamous epithelium. Occasionally, however, the entire length of the ducts is covered by squamous cell epithelium. Whether this be, as some claim, the result of an inflammatory metaplasia whereby the columnar or transitional epithelium is replaced by a well-developed layer of the squamous cell epithelium, as is frequently noted in small areas in the cervix and uterine cavity is as yet an open question. This view is championed by K. Touton, G. Nobels, and by Sitzenfrey, all of whom have described ducts lined by squamous cell epithelium in cases with gonorrheal Bartholinitis. Cancers developing from areas in the duct lined by squamous cell epithelium, naturally will be squamous cell epitheliomas. This type of cancer, when seen in advanced growths, may not be differentiated from the more common vulvar carcinoma.

Etiology.—The same theories which are advanced for carcinoma in general apply to cancer in Bartholin glands. Many have emphasized the fact that the great majority of the cancers of the Bartholin glands had had previous gonorrheal infections; although we may remark in passing that were gonorrheal infection of Bartholin glands the chief etiological factor, there would be millions of such cancers rather than the dozens which have been recorded. Eden quotes a case of a woman who had an abscess on the left labium which drained for one and a half years, when a lump appeared in the same region which was proved to be adenocarcinoma. Kelly's case appears to have developed on an inflammatory basis. It was first incised under the impression that it

was an abscess, which idea was confirmed by the large quantity of cheesy, bloodstained débris which escaped with clots. The first suggestion of the carcinomatous nature did not present until her return four months later.

Age.—The carcinoma usually appears after the menopause. Spencer and Wittkopf each have reported a case of the disease in women under thirty, both of whom had had a gonorrheal infection of the gland. Our case was forty-eight years.

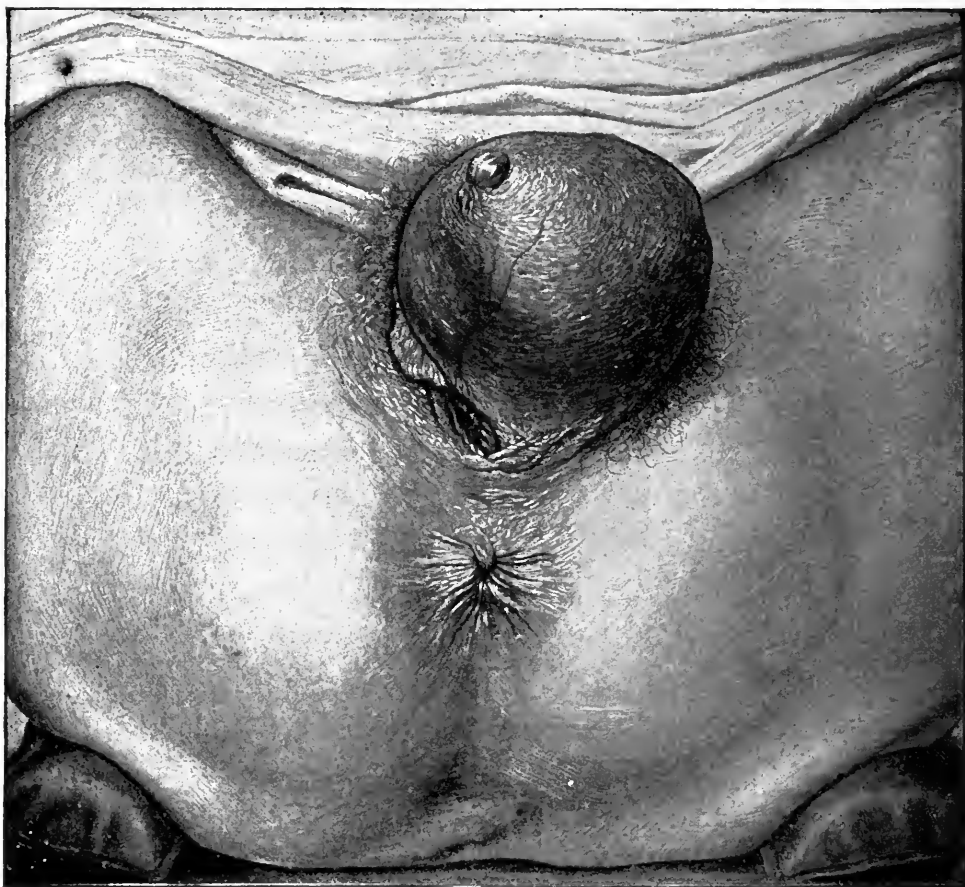


FIG. 14.—CARCINOMA BARTHOLIN GLAND (Kelly, Operative Gynecology).

Gross appearance.—The tumor varies in size from a small pea-sized nodule to a cauliflower mass even larger than a goose egg (Fig. 14). It is usually firm and nodular but may be soft and suggest an abscess, probably as a result of bacterial invasion. The smaller growths are usually red (from inflammatory reaction), but have been described as blue with large skin veins surmounting the tumor. Ulceration usually occurs early, and the growth presents the typical appearance of a car-

cinomatous ulcer, with its punched-out edges and a necrotic sloughing base. The edges are firm, and the tumor bleeds readily. With the coming of ulceration, the surrounding tissues become infiltrated, and the mass becomes firmly attached to the underlying pubic bones. The glands are early involved, and enlarge not only from carcinomatous invasion but especially from the inflammatory reaction. Either side is attacked with equal frequency. The growth may be primary in both sides, or, as shown by the case of Schluter, both sides may be involved secondarily from extensions from a cancer of the uterine body.

Symptoms.—Subjective symptoms may be absent when the growth is small, especially if the skin is intact. Occasionally there is dull pain. With the advent of ulceration, the pain may be acute, lancinating in character, and worse when walking, or during menstruation. Purulent leukorrhea may be present, usually attributed to a discharging abscess. Hemorrhage following trauma may first draw the patient's attention to the growth, as in the case of Wittkopf.

Diagnosis.—The diagnosis of malignancy is usually easy but may be most difficult as in the case of Kelly. The fixed growth, ulceration, involvement of glands are typical when present. It may be difficult to differentiate late growths from cancers of other structures. Gottschalk, Eberth, Koppe and others have emphasized the fact that there are other adenoid elements than the Bartholin glands in the pelvis, due probably to misplacements of epithelial elements in early embryonic life from which adenocarcinoma may arise. The location of the tumor and its low-power microscopic picture will usually give the diagnosis in the early cases of adenocarcinoma, since the growth tends to simulate atypically the outlines of the original gland. The diagnosis may not be made in the squamous cell carcinoma which originates in the ducts unless the surrounding skin is free from carcinoma. This usually is easily demonstrated in the early cases.

Prognosis.—The prognosis is most gloomy, irrespective of treatment. It is usually said that no case in literature has survived the five-year period without evidence of local or glandular recurrence. Yet any one who turns to the literature will be amazed at the paucity of follow-up notes. Several record their cases as clinically cured after one or two years. It is high time that all recognize that five years of freedom from recurrence is the minimum that may be counted as cure.

Metastasis is primarily to the external inguinal glands. There is a cross system whereby glands of the groin of the opposite side may be involved. At the same time, the growth drains to the pelvis, and the iliac glands are often involved. The pelvic bones are early affected and metastasis may be widespread.

Treatment.—The treatment is that of other vulvar cancers (q. v.).

SARCOMA OF THE VULVA

Primary sarcoma of the vulva is an exceedingly rare condition and is usually briefly discussed, if mentioned at all, in gynecological textbooks. Veit, in discussing this tumor, states that it is so rare that it is difficult to establish its clinical picture.

In contrast to the primary sarcoma, there have been described a number of secondary vulvar sarcomata which have resulted from the extension of growths primary in the vagina or pelvic connective tissues or from sarcomatous changes in vulvar fibroids (q. v.). They will not be considered under this section. The following deals with primary sarcomatous growths of the vulva.

Classification.—Vulvar sarcomata may be pigmented (melanosarcomata), or nonpigmented, and are composed of round, spindle or mixed cells. Occasionally a melanotic tumor presents a cell picture which is so atypical that there may be difficulty in determining whether the growth is sarcoma or carcinoma. Such tumor usually shows an alveolar structure. Further difficulty has arisen in the classification of a small group of tumors which usually appear first without color and far later, and occasionally only in the local recurrence after operation, exhibit the typical deep, blackish-brown pigmentation of the melanomata. These properly belong to the melanotic division, since Ribbert has shown that there may be colorless primary melanosarcomata.

Frequency.—The rarity of this disease is shown by many authors. Eiselt reviewed 104 melanomata (both sarcoma and carcinoma) reporting the literature from 1806 to 1861 without finding one developing in the external genitalia. Dieterich, who continued Eiselt's tabulation up to 1887, found 11 vulvar melanotic sarcomata in the review of 249 melanomata. None of the 483 sarcomata in the widely quoted statistics of Gurlt are vulvar. Caruso, in 1889, collected 28 vulvar sarcomata, 12 of which are melanotic, yet Blair Bell in reviewing this series of reported cases reduced the list considerably by exclusions warranted by the study of the various individual case reports. Torgler, in 1900, stated that there were 52 primary vulvar sarcomata reported in the literature and abstracted the histories of 20 melanotic cases. It is quite possible that his list contains many doubtful cases, since Blair Bell, in 1907, in a fairly exhaustive report, was able to find but 21 cases of primary nonpigmented vulvar sarcomata. P. Meyer, in 1908, cites 39 sarcomata of the vulva, although it appears to us that he includes several melanocarcinomata. Veit, in 1909, states that 35 cases of nonpigmented growths have been reported together with the same number of pigmented sarcomata. Yet we find in this series several cases which at least appear to be more properly sarcomatous changes in vulvar fibroids of which, there are now many re-

ported cases in the literature. In 1913, Voigt was able to find only 9 cases of melanosarcomata of the clitoris.

Textbooks usually state—probably quoting from Veit—that the majority of vulvar sarcomata are melanotic but we cannot find on what authority. The tabulations of Caruso and Torggler, which are the largest recorded, show respectively 12 melanotic sarcomata in a series of 28 vulvar sarcomata, and 20 melanomata in a total series of 52 vulvar sarcomata.

Etiology.—Little is actually known concerning the etiology, although it would appear as if nearly every possible theory had been advanced to explain the origin. Heredity is not proved. Some, when considering the etiology of the melanotic sarcoma, have thought, as Wagner, that possibly blondes were more likely to be affected, an idea prompted by the fact that in horses, the white horse alone appeared to be predisposed to melanotic tumors. The literature unfortunately does not permit of chance for corroboration, since the complexion of the patient is seldom given, although several cases have been cited in the negro.

Trauma does not appear to be an important predisposing factor for sarcoma of the vulva, since the vulva has been developed by nature to withstand much trauma. This point appears well proved when we consider the inevitable trauma of labor and the fact that the vulva is especially resistant to infections.

Age.—In marked contrast to sarcoma in general which is often a disease of youth, the vaginal sarcoma usually develops in later life. The age incidence in 18 nonpigmented vulvar sarcomata collected by Bell is as follows:

Under	10	years.....	1 case
Between	18-30	"	5 cases
"	30-50	"	9 "
"	50-70	"	3 "

The melanotic tumors are noted in even older women. Torggler's cases, in which the youngest was thirty-seven years and the oldest seventy-two, present the following:

Between	30-40	years.....	1 case
"	40-50	"	3 cases
"	50-60	"	5 "
"	60-70	"	4 "
More than	70	"	3 "

Meyer's series of 30 melanomata in which some melanotic carcinomata are probably included gives:

Between 20-30 years.....	1 case
“ 30-40 “	2 cases
“ 40-50 “	5 “
“ 50-60 “	12 “
“ 60-70 “	8 “
“ 70-80 “	2 “

The ages were given in 6 of Vogt's 9 cases of melanotic-sarcoma of the clitoris as 37, 48, 51, 57, and 70 years.

Point of Origin.—The tumor may develop from any vulvar tissue of mesodermic origin or from the periosteum of the bones which underly the external genitalia.

There has been much discussion as to the exact point of origin of the melanotic sarcomata. Obviously they must develop from cells containing pigment. There are a great number of possibilities, although it would appear that they may develop from any chromophore. Unna claimed that these tumors develop from pigmented soft nævi. Weiner also sought their origin in pigmented moles or warts. Dietrich in this connection found that 37 of 145 melanosarcomata of various parts of the body had had pigmented nævi as a possible site of origin, as did Just in a smaller series in which it would appear that 23 of 54 melanotic skin tumors also developed from moles. Von Rave collected 55 melanomata which developed from pigmented warts but none of his cases were vulvar growths. On the other hand, Torggler states that he could not determine any relationship between nævi and the melanosarcomata which he reported or reviewed.

There is no doubt but that there are many pigmented cells in the external genitalia, and that these increase in number during pregnancy, or as the result of certain chronic inflammations as intertrigo, etc. Veit saw in these the origin of the melanotic sarcoma. There are, however, other pigmented areas in the body from which melanotic tumors might develop but do not appear to do so. Thus, Torggler calls attention to the fact that no melanotic sarcoma has been described which originated in the pigmented areas about the nipple which contains darker cells than other parts of the skin surfaces.

Location and Appearance of Growth.—The majority of the vulvar sarcomata develop in the labia, after which the growths in the clitoris and urethra follow in order of frequency. Twelve of the 20 melanotic sarcomata collected by Torggler were labial, 4 were on the clitoris and 1 each on the urethra, mons and perineum. Fourteen of Bell's series of 21 nonpigmented cases were labial, with 3 each on the urethra and clitoris and 1 on the vestibule. The exact point of origin, however, is often difficult to determine with accuracy in cases which come late for treatment. Sängner noted a case in the hymen.

In appearance, as long as the tumor is not ulcerated, it may re-

semble either the vulvar fibroma or lipoma. It is round or oval with the long axis parallel to that of the labia and often contains nodules. It may be sharply circumscribed. Sometimes, on the contrary, it has a diffuse border. Occasionally it is pedunculated; the growths of the

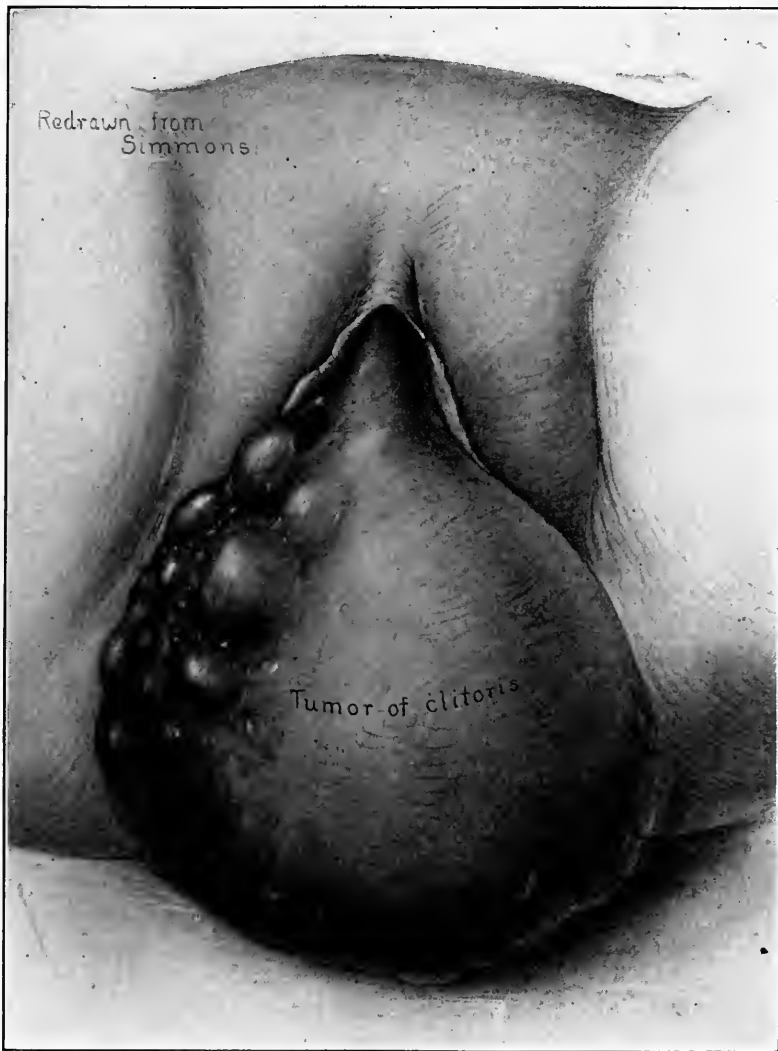


FIG. 15.—SARCOMA CLITORIS (redrawn from Simmons).

clitoris are usually so (Fig. 15). It is not tender and is firmly fixed. Ulceration to the deeper structures occurs after a variable interval, and the growth becomes fungated. The pigmented forms present light brown to greenish black in color. The surrounding skin is unchanged at first and may move freely upon the growth. Later it is fixed and may be edematous.

The tumor usually grows with astonishing rapidity, although occasionally it remains latent for a considerable period.

Metastasis.—Metastasis usually occurs early and through the lymphatics. Later the cells break through into the blood stream and involve even the most distant organs. None appear to be immune, and metastases in the liver, stomach, intestines, ovary, lung, heart, brain and kidney have been described. The neighboring bones may be affected. The adjacent lymph glands may enlarge to tremendous size, especially in the melanotic types. Glandular involvement in the groin the size of two fists is not uncommon. The chain of glands nearest the tumor absorb most of the pigment until metastasis is fairly general.

Clinical Picture.—Martin, who, in 1913, reviewed the sarcoma of the labia majora reported in the literature, gives the following picture:

There is a first stage which may last for years, when there is only a small indolent nodule or a more or less pigmented *nævus*. During the second stage, there is a more or less rapid growth of the tumor, which becomes troublesome, but not painful. In the third stage, there is a tendency to spread to the inguinal glands, to the labia of the other side, to the clitoris and muscles. Presently there is compression of the saphenous and femoral vessels, resulting in edema, and finally in metastasis and death.

Symptoms.—The symptoms are similar to those of other vulvar neoplasms, namely, itching, burning, dysuria, and a sense of weight or pressure in the pelvis. Discharge, usually foul, may be present, and bleeding on slight touch is common. Hemorrhage may be very profuse and be the cause of exitus. In melanotic sarcoma, the mucous membranes may become discolored and melanin may be excreted in the urine, especially if the kidneys are involved in metastasis. If the pigment is excreted as melanin, the urine is dark. Melanogen causes but little darkening of the urine. On standing, however, the pigment is oxidized with resulting deepening of color. A melanemia may occur in case of general spread of melanotic elements in the body.

Diagnosis.—The diagnosis can be made only with the microscope, although there is usually no doubt of the malignancy of the well-developed tumor.

Treatment.—The treatment is wide removal, made as early as possible, of the vulva and inguinal lymphatics in one piece by a careful and wide dissection—the same as in vulvar carcinoma (*q. v.*). X-ray has not given results. Radium is yet untried in any series of cases.

Prognosis.—The prognosis is grave. Death appears to result uniformly in cases in which the diagnosis of vulvar sarcoma is firmly established. There are only 2 cases in the literature which appear in contrast to the rule that death follows from a few months to a year following diagnosis: Fergusson's case of a pigmented tumor of the mons reported in 1851 which did not present recurrence until two

years after removal; and Fischer's case of perineal tumor with masses in the inguinal region the size of two fists which remained twenty years before recurrence and then survived a second operation for twelve years. The dates of these reports, 1851 and 1881, suggest at least the chance of error in diagnosis.

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CHAPTER III

BENIGN TUMORS OF VAGINA

Cysts of vagina—Frequency—Classification—Etiology—Age—Point of origin—Location and appearance—Histology—Types of cysts—Epithelial inclusion cysts—Cysts of vaginal glands—Cysts of Gärtner's Ducts—Cysts of Müller's Ducts—Cysts of ureter—Cysts of urethral gland—Gas cysts—Echinococcus cysts—Symptoms—Diagnosis—Differential diagnosis—Treatment—Fibroma of the vagina—Etiology—Age—Site of origin—Classification—Location—Form, size and appearance—Histology—Occurrence with pregnancy—Symptoms—Diagnosis—Treatment—Prognosis—Literature.

CYSTS OF VAGINA

Vaginal tumors are even more rare than vulvar neoplasms. Of these, vaginal cysts are by far the most common. They develop, as their name implies, in the vaginal wall, and are of interest chiefly from the standpoint of etiology and classification, since vaginal cysts which occasion clinical symptoms are extremely rare.

Cysts of the vagina were described as early as 1765 by Haller and^{*} at about the same time by Morgagni. Both observers, however, incorrectly considered them hydatids. The observation of Oakley Heming in 1830 is widely quoted, yet it appears that Hugier, in 1847, first advanced the theory that they arose from vaginal glands. Hugier based his belief on the supposition that there were two sets of vaginal glands, the superficial, and the deep. (The question as to whether the vagina contains glands has not been settled even at the present time.) Hugier, however, believed that the superficial glands opened into the lower part of the vagina, and occasionally gave rise to thin-walled, superficial cysts which often were multiple. The deeper glands had no outlet and were truly closed follicles. Under certain conditions in which trauma was a factor, they developed into thick-walled cysts. Eleven years later, Charière came to rather similar conclusions, but thought that the most common cause was mechanical injury to vaginal tissue. The subject remained in complete confusion until Winckel, in 1871, collected 50 cases of vaginal cysts from the literature and presented a critical and careful study based on anatomical facts. Baumgarten, in 1887, showed that the histological picture aided in determining the various sources of origin of the cysts. In America, the work of Stokes, in 1898, and of Cullen, in 1905, has done much to elucidate many of the perplexing points of the question.

Frequency.—Gurlt found only 3 cases in his tabulation of 11,140 tumors in women. Yet vaginal cysts are far more common than the literature indicates, if we include in our definition the very small cysts which give no symptoms and which are discovered only accidentally. Cysts of large size are very rare. Only a few have been as large as an orange. Only 14 were the size of a hen's egg, or larger, in the 50 cases collected by Winckel in the literature from 1830 to 1871. Stokes, in 1898, reported 10 cases in 5,000 gynecologic cases in the Johns Hopkins Hospital. Cullen, in 1905, reported 53 cases observed during the ten-year period from 1893 to 1904 in the same clinic. To complete the series, he included Stokes' cases in his report. Only 10 cysts were the diameter of an inch or larger.

Classification.—Under the heading of vaginal cysts are grouped together a number of primarily benign cystic tumors of different origin and of varying size, appearance and location. Some, as J. Veit, and Stokes, have objected to classing as vaginal cysts the larger tumors which develop from embryological remnants in structures adjacent to the vagina, and which are forced down into the vagina as they grow. The objection is made that such tumors cannot be brought into an etiological classification with the true vaginal cysts. Practically, however, for clinical purposes we must regard any cyst which presents in the vagina as a vaginal cyst.

Etiology.—Trauma, obstetrical or surgical, is chiefly responsible for the cysts which result because of the inclusion, during repair operations, of small areas of vaginal epithelium in the depths of the wound (Fig. 16).

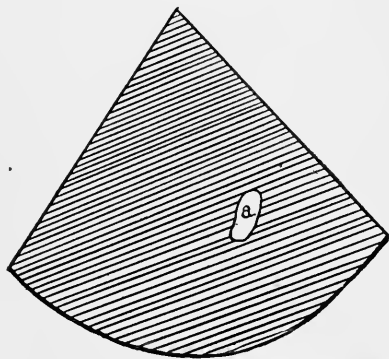


FIG. 16.—INCOMPLETE DENUDATION IN PERINEORRHAPHY FROM WHICH CYST MAY ARISE.

We are ignorant of the causes which excite the growth into cysts of glands included within the vagina, and of the embryologic remnants which are normally present in the vaginal wall.

Age.—The great majority of cases are noted during the child-bearing age, yet they occur at any time of life.

Point of Origin.—Usually the point of origin can be determined by histological study. Vaginal cysts may arise from

- (a) Inclusions of vaginal epithelium.
- (b) Aberrent vaginal glands.
- (c) Gärtner's duct.
- (d) Müllerian duct.
- (e) Lymphatics.

Location and Appearance.—Cysts may develop in any part of the vagina, yet there are certain parts where they are more commonly found. Stokes states that cysts of the posterior vaginal wall generally lie in the median line; if in the lateral vaginal wall they present usually in the sulcus at the junction of the lateral and posterior wall. Cysts in the anterior wall are more common under the urethra, or on either side. Some authors claim that they are more frequently found on the right than on the left lateral wall.

Small cysts often suggest a white grape in appearance, yet vary considerably according to the thickness of the wall, the character of their contents, and the depth in which they lie in the tissue. The wall may be thin or thick, and may contain clear, milky, or thick, tenacious, chocolate-colored fluid. The larger cysts are often egg-shape, with the long axis parallel to the long axis of the vagina. Their color may be pale or opaque, depending largely upon the type of their contents and the thickness of the wall.

The position of the cyst is of some value in deciding its etiology. For example, a cyst of the posterior wall cannot arise from a dilatation of the duct of Gärtner, since this type lies in the lateral vaginal wall. A cyst following the course of the vagina, or winding about it, suggests an origin from müllerian tissue.

Histology.—The histological picture varies according to the structures from which the tumor has originated. Since glands may arise from inclusions of stratified epithelium, or from embryological remnants containing cuboidal epithelium, or from lymphatics, it follows that the lining of the cysts may present different cell pictures. Thus, ciliated columnar epithelium, low cuboidal, or stratified squamous epithelium may constitute the lining. Occasionally, cysts are lined with squamous epithelial cells, the superficial layers of which are vacuolated and devoid of nuclei. Other cysts may be found which contain both cuboidal and squamous cell epithelium in their lining membrane. These cases develop from ducts or glands which are lined by cylindrical epithelium, although the neck of the duct or gland ends in squamous epithelium. Other cysts may not present an epithelial lining, the cells having been killed by pressure atrophy.

The cyst contents vary from clear serous to turbid and even hemorrhagic material; calcareous deposits have been found in the walls

(vaginal calculi). The consistency and appearance of the cyst contents depend upon the amount and type of the solid substances suspended in solution. Desquamated epithelium, fatty débris, cholesterolin crystals, and blood have been found in the fluid.

Types of Cysts—**EPITHELIAL INCLUSION CYSTS**.—By far the largest number of vaginal cysts have developed from tags of vaginal mucosa, which

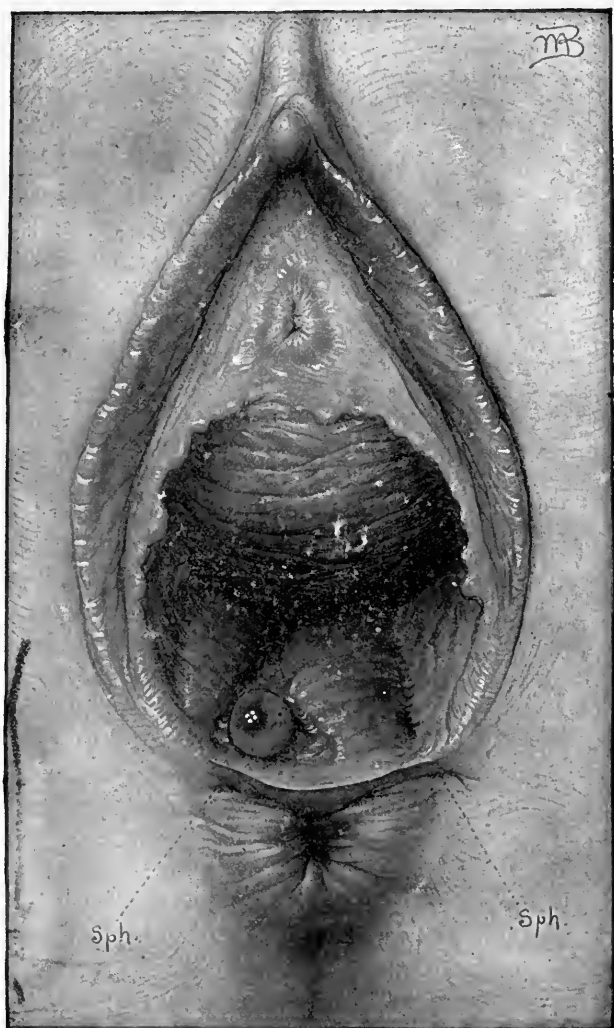


FIG. 17.—VAGINAL INCLUSION CYST (Kelly, Operative Gynecology).

were buried in the repair of vaginal tears following labor or from faulty denudation in secondary vaginal repairs (Fig. 16). They may also follow adhesive vaginitis from any cause which results in abrasions of the surfaces of the vagina, so that agglutination follows. Usually they are small, ranging in size from a few millimeters to 2 or 3 centimeters, and generally are single.

They are found most often in the posterior or lower lateral walls of the vagina, frequently at the site of an old tear. They are yellow or white in color, and have thin, smooth walls from 2 to 3 millimeters in thickness. The inner surface is smooth. They contain a friable material, of yellow color, which slightly resembles pus, but which actually consists of exfoliated squamous epithelium (Fig. 17).

Histologically, the vaginal mucosa attached to the cyst is usually normal, yet may be atrophic from pressure of the cyst. The cyst walls are of fibrous tissue, lined by a varying number of cells of squamous epithelium. The epithelial covering ranges from two to thirty layers of cells (Cullen) and occasionally is of uniform thickness throughout, yet more often contains thick and thin areas. The superficial epithelial layers contain no nuclei and the cells are vacuolated. The deepest layer is cuboidal.

CYSTS ARISING FROM VAGINAL GLANDS.—The existence of vaginal glands has been much questioned. Eppinger, Nagel, Gebhard, Pretti, Waldeyer, Williams, and others deny their existence. Nor have we ever seen them in the examination of a large number of specimens. On the other hand, Hennig described them in 1870, and von Preuschen in 1877 found definite glands in the vagina in 4 of the 36 bodies which he examined. Cullen also states that they are occasionally met with.

Yet glands which are found so rarely cannot be considered as a constant structure of the vagina. Von Preuschen, as a result of his study, stated that the vaginal glands seen by him presented a structure rather similar to the sebaceous glands of the vulva, consisting of a broad, baylike portion, together with several fingerlike tributaries which were filled with a dull, glistening mass resembling fat. The main portion of the gland, the baylike formation, is lined with squamous epithelium. In the tributaries which lie deeper in the vagina, the superficial layers of the squamous epithelium have disappeared, and the lining of these smaller glands is of ciliated cylindrical epithelium.

The structures described by von Preuschen lie in the upper portion of the vagina. Since they have been sought so unsuccessfully by so many others and were found by von Preuschen in only 4 of his 36 cases, the majority of gynecologic pathologists class most of these structures as aberrant-cervical glands. The cases of Cullen, however, are more difficult to dispose of. The similarity of Hugier's and von Preuschen's observations are worthy of comment.

Cullen feels that three of the cysts described by him, and, possibly a fourth, were derived from vaginal glands. The 3 cases were noted in young women who had perineal lacerations for which they had come for operation. The cysts were found in the resected mucosa of the posterior vaginal wall, lying by the side of definite inclusion cysts. The cysts were small, from 6 millimeters to 1.5 centimeters in size and were lined by cuboidal epithelium, which was flattened in 2 of the 3 cases. The cysts contained mucus, with no evidence of desquamated epithelium which Cullen believes would

surely have been present had the cysts been lined primarily with squamous epithelium. Stokes also reports a case removed by C. P. Noble because of symptoms, in which the cyst was 8 by 5 centimeters and was lined by a single layer of high columnar epithelium, which Stokes believes was a true prototype of that found in the cervix.

CYSTS OF GÄRTNER'S DUCTS.—Gärtner's ducts in the embryo may be traced from the parovarian tubules (wolffian body) in the mesosalpinx down through the broad ligament, either in or at the side of the uterus, down as far as the cervix. From here it may extend down either to the anterior or the lateral wall of the vagina, and even as far as the outlet. On cross section, the duct shows an outer covering of fibrous tissue, a middle zone of smooth muscles arranged longitudinally and transversely, and an inner lining of simple cuboidal or cylindrical epithelium. In the majority of cases, the duct disappears, but, in a few instances, portions or all of the duct persist in adult life. As the result of accumulated secretions, the duct may become cystic. If only one segment of the duct persists, dilatation gives rise to a single cyst; if several patent segments of the duct are separated by atretic portions, multiple cysts may develop. These ducts are usually small and may suggest a string of beads, as did the case of Debierre. In rare instances, the duct may be patent from the parovarium to the vagina, and cystic dilatation may give rise to a mass extending up into the broad ligament and occasionally down beneath the vagina. Cysts of this type may be as large as a child's head. They are very rare.

Cysts originating from the portion of Gärtner's duct situated in the vaginal wall are comparatively frequent, and lie in the anterior or lateral vaginal wall (Fig. 18). They may be exceedingly small but usually are several centimeters in size. Usually they are not perfectly globular but cylindric or funnel-shaped, corresponding to the long axis of the vagina. The cyst walls are of variable thickness (1 to 2 millimeters) and contain clear or straw-colored fluid. Histologically, the walls are made up of fibrous and muscle tissue and are lined with cylindric or cuboidal epithelium. The overlying vaginal mucosa may be atrophic. A small stem may be seen leading from the cyst, probably representing a more rigid portion of the duct (Cullen).

CYSTS ARISING FROM MÜLLER'S DUCTS.—Cysts arising from this source are present only when the two müllerian ducts failed to meet. As a result, there are two uteri and two vaginae. Cysts can only arise when one vagina is well developed and the other is represented only by a rudimentary cord which becomes fused in the wall of the well-developed vagina. Secretions accumulating in the atrophic vaginal tube cause a cystic dilatation which appears to spring from the lateral vaginal wall (Fig. 19).

Occasionally both uteri are fairly well developed, yet one vagina has no lower outlet, and is in reality only a blind sac. With menstruation, there results a cyst containing menstrual fluid which gradually becomes chocolate brown in color. Freund, in 1877, called attention to this deformity, and

since then Kleinwächter has collected other cases. The tension of the cyst is sometimes sufficient to break the lower wall of the sac so that the fluid may drain through the developed vagina. Infection may be present before the cyst opens (Fig. 20).

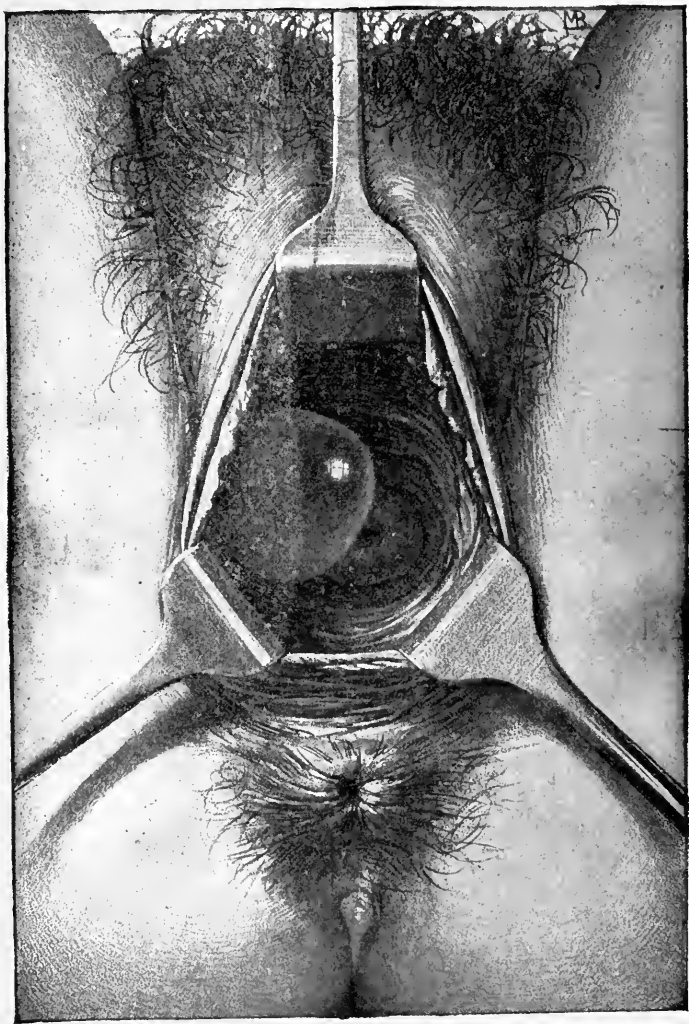


FIG. 18.—CYST IN VAGINA (Kelly, Operative Gynecology).

CYSTS DEVELOPING FROM THE URETER.—Cysts originating from a pouch of a misplaced ureter are occasionally met with, from which urine escapes when opened. Occasionally, as a result of trauma, fistulous openings are seen through which urine is discharging. Such cases are usually seen when two kidneys or two ureters exist on one side. Broedel has shown that when this state exists, the ureter from the lower kidney is more apt to be

inserted in the normal site than is the other one. The ureter of the upper kidney is apt to be carried down further with the wolffian duct to empty more mesially near the internal urethral orifice, while occasionally it forms a blind sac.

CYSTS ARISING FROM URETHRAL GLANDS.—Cullen thinks it unlikely that cysts develop from urethral glands, although the possibility cannot be denied. The cases which appear to arise from such structures may equally well be ascribed to remnants of Gärtner's ducts unless a connection with the

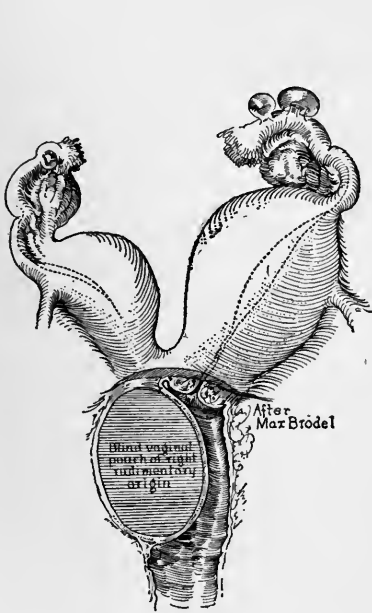


FIG. 19.

FIG. 19.—VAGINAL CYST ARISING FROM IMPERFECT UNION OF MÜLLER'S DUCT.
(Schematic after Cullen.)

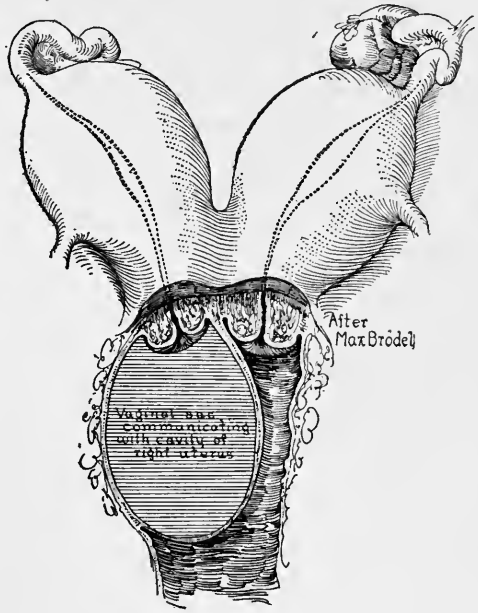


FIG. 20.

FIG. 20.—VAGINAL CYST REPRESENTING IMPERFORATE AND RUDIMENTARY VAGINA
OF RIGHT SIDE.

urethra can be proved. The lining of these cysts (usually small) is made up of several layers (three to eight) of cylindrical cells lying upon flattened cells which take a deep stain.

GAS CYSTS.—Various names have been advanced to designate these rare cysts which are usually observed during pregnancy. Winckel termed them colpophyperplasia cystica, Eppinger designated them as emphysema vagina, and Ruge called them colpitis vesicula emphysematosa.

They were described by Braun in 1861 and ten years later by Winckel, who reported 3 cases, since when they have been reported occasionally. They are usually small, superficial, transparent, thin-wall cysts, closely grouped together on the injected swollen anterior or posterior walls. There were a great number of tiny cysts in one of Winckel's cases, so closely packed together "that a dollar would cover 15 or 20." The cyst wall is a

thin layer of connective tissue without a lining of epithelium. On puncture, gas escapes with an audible noise. There is no fluid in the cavity. Eisenlohr believes that these little cysts are due to some gas-producing organism which develops in the lymphatics. We know nothing positive about their true origin. They disappear spontaneously during the puerperium.

ECHINOCOCCUS CYSTS.—Echinococcus cysts may develop in the vaginorectal septum and project into the vagina. Occasionally they attain considerable size. The echinococcus can be demonstrated in the cyst with the microscope.

Symptoms.—The smaller cysts rarely cause symptoms, and as a rule are discovered accidentally. The larger cysts may give symptoms from pressure and occasionally offer obstruction to both coitus and labor. Cysts of the posterior wall may roll out the pelvic floor and simulate prolapse. The larger cysts have occasionally formed an efficient barrier to birth. Güder reported 3 such cases and collected 20 others from the literature in 1889, several of them being echinococcus cysts. The case of Peters is especially worthy of comment. In this case, one pound of clear fluid was removed from the cyst with a trocar before the walls collapsed sufficiently to allow advance of the child's head. The large cysts which extend up into the broad ligament give rise to various symptoms depending upon the size and position of the growth. The tumor may make pressure on the uterus, ureter, bladder and rectum and nerves of the pelvis. They may give rise to bearing-down sensations and may even interfere with locomotion. The cysts are not tender.

Diagnosis.—There should be little difficulty in the diagnosis provided the physician proceeds in a methodical manner. These tumors usually grow very slowly, although they may enlarge rapidly during pregnancy. They tend to grow in the direction of least resistance, consequently, they may grow along in the rectovaginal septum, before developing in the cavity of the vagina or the rectum. They may indeed grow away from the vagina into the broad ligament until they encounter resistance sufficient to force the growth downward.

The cysts usually feel soft and elastic, and give the sensation of fluctuation, yet when greatly distended they may be so firm and resistant that they suggest a fibroid. The physician will do well to examine first with a speculum before making the bimanual and rectovaginal examination.

Differential Diagnosis.—These cysts may be confused with soft vaginal fibroids, cystocele, rectocele, hernias, and hydrocele of the canal of Nuck.

Treatment.—The treatment is excision in all cases. The smaller cysts can readily be removed and the cavity sutured with chromic catgut. The removal of the larger vaginal cysts may be difficult because of lack of exposure and the presence of hemorrhage. Occasionally, it is

more wise to remove part of the growth and unite the remaining edges with the vagina, so that eventually the part of the cyst wall that is left becomes part of the vagina. The larger vaginoparovarian type of cyst may present interesting surgical problems, and abdominal operations are usually necessary. Occasionally it may be quite impossible to remove the sac. The growth may then be treated with marsupialization. One should always keep in mind that swellings in the anterior vaginal wall may prove to be a dilated blind ureter, the incision of which may create a urinary fistula.

FIBROMYOMA OF THE VAGINA

Fibromyoma rarely originates in the vagina. Breisky, in 1886, collected 58 cases; Smith, in 1902, 100 cases; and Potel, in 1903, extended the list to 150 cases. Müller, in 1914, and Giesecke, in 1915, have made careful studies, the latter author citing 196 cases.

Etiology.—The causal factors are not known. The same theories which have been advanced to explain uterine fibroids and the adenomyoma (q. v.) obtain here.

Age.—The majority of cases are noted in the third and fourth decades. Cases in children have been observed, although there is doubt as to whether they are true fibroids. Many state that they belong to the sarcoma or teratoma. Martin observed a case in a newborn child. Tratzels' case was fifteen months old. Wilson's case was two and one-half years.

Site of Origin.—The fibroid tumors develop from the connective tissue of the vaginal wall, or from the coats of the musculature. Many claim that the growths which develop from the cross-striated muscle usually belong to the sarcoma.

Classification.—Fibroids which have their origin in the uterus, but which have grown down into the connective tissue and are forcing their way into the vagina, are excluded from the classification. In the same manner, pedunculated growths from the cervix which have become adherent to the vagina do not belong to this category. Here belong only such growths as have originated in the structures of the vagina.

Properly speaking, the tumors may be fibroids, myomata, or fibromyomata, depending upon the character of their prevailing tissue. Practically they are all grouped as fibroids. The adenomyomata, however, form a distinct division and are considered separately.

Location.—The vaginal fibroids, like the sarcoma, usually develop on the anterior vaginal wall, in contrast to the carcinoma which develops on the posterior wall.

Form, Size and Appearance.—The tumors are usually single, but may be multiple. They consist of hard, round, nodular tumors, which,

though usually of small size, may attain considerable dimensions, even more than five or six inches in diameter. Emmel's case weighed 625 grams. They grow from beneath the mucosa into the vagina, and in consequence, finally develop a pedicle, if they are not removed prior to that stage. Usually, they are encompassed by a fibrous capsule. They are covered by the vaginal mucosa on their vaginal surface, which is often excoriated or ulcerated, following friction. The cut surfaces present the typical fibroid appearance, and often present macroscopic evidence of degenerations.

Histology.—Histologically the tumor is made up of smooth muscle bundles and connective tissue in variable proportions. Degenerations are common, similar to those of uterine fibroids (q. v.). Edema is so frequent as nearly to constitute the rule in the larger tumors.

Complications.—The tumor may undergo various degenerations from which symptoms may occur. Sarcomatous changes have been noted.

Occurrence with Pregnancy.—The growth is an occasional accompaniment of pregnancy. It may enlarge tremendously from edema as well as actual hypertrophy, just as do uterine fibroids. A series of vaginal fibroids and pregnancy has been collected by Güder, in which there was 1 spontaneous birth in the presence of the tumor, 3 forceps, 2 versions, 1 breech extraction and 3 cesareans. The tumor was removed before labor in four instances, and once shortly before birth which resulted spontaneously.

Symptoms.—Usually there are no symptoms in the smaller growths which are found accidentally, unless the tumor has become ulcerated and has occasioned a foul-smelling leukorrhea. Da Costa described a case which projected from the vulva and measured 6 by 4.5 inches. Simpson's case was the size of two fists and interfered with micturition and the escape of the uterine discharges. As a rule, the larger growths cause bearing-down pains and pelvic pressure symptoms, especially upon the bladder and rectum. Dyspareunia is common.

Diagnosis.—The diagnosis is readily apparent in the very great majority of cases. It may be difficult in cases which block the vagina, where the site cannot be ascertained, since the pedicle cannot be reached. There is usually no doubt that the tumor is a fibroid. The differential diagnosis is made chiefly from vaginal cysts.

Treatment.—The treatment is surgical removal, which usually occasions no difficulty. Pedunculated tumors are easily ligated and removed, after which the vaginal edges are brought smoothly together. The sessile tumors are removed after exposure through a linear incision when the tumor is shelled out from its capsule. The hemorrhage should be controlled and the raw edges brought together with chromic catgut. A vaginal pack promotes healing if left in for twenty-four hours.

The larger growths may be difficult to expose, and episiotomy or even a large paravaginal incision may be found necessary. Healing is usually by first intention if there was proper wound approximation. There are, however, numerous instances of infection.

Prognosis.—The prognosis is good. The growth does not recur.

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CHAPTER IV

MALIGNANT TUMORS OF VAGINA

Carcinoma of vagina—Frequency—Etiology—Classification—Location—Primary growths, appearance and form—Histology—Method of growth—Complications with pregnancy—Symptoms—Diagnosis—Prognosis—Sarcoma of vagina—Classification—Sarcoma in infancy—Etiology—Age—Point of origin—Location—Appearance—Method of growth—Histology—Symptoms—Duration—Diagnosis—Prognosis—Therapy—Sarcoma of adult—Classification—Etiology—Age—Appearance—Location—Histology—Method of growth—Symptoms—Diagnosis—Prognosis—Treatment—Radium—Literature.

CARCINOMA OF THE VAGINA

Carcinoma of the vagina may be primary or secondary.

Primary carcinoma is rare. Various attempts have been made to determine its frequency, as may be seen by the following:

In 59,600 cases, Gurlt found 114 carcinoma of the vagina (.19 per cent).

In 35,807 gynecologic patients in Berlin, Schwarz found 84 (.24 per cent).

In 10,000 gynecologic patients in Berlin, Hofmeier found .11 per cent.

In 18,000 gynecologic patients in Halle, Rohde found .06 per cent.

In 8,981 gynecologic patients in Prague, 1875 to 1891, there were 38 cases (.42 per cent).

It was found 14 times in 8,287 women (.16 per cent) who died of cancer in France (Beigel).

Gurlt's statistics show 1.5 per cent in 7,479 carcinomatous women; and .77 per cent (15 cases) of 1,924 carcinomatous women in Vienna. Williams states that it formed .43 per cent of the carcinoma in his series.

Friedl found it once for every 63 uterine carcinomata in Vienna and Prague. He also expressed the belief that primary carcinoma may be more frequent than is usually considered for the following reason: The cancer usually begins on the posterior vaginal wall very close to the vaginal portion of the cervix. Its tendency in growth is to extend up to the posterior cervix. Thus a late growth coming late to treatment in which the cervix has been widely involved by extension from the vaginal tumor is extremely likely to be diagnosed as vaginal involvement secondary to an inoperable cervical cancer.

Etiology.—Nothing is known as to the cause of this affection. Heredity and trauma during childbirth have not been shown to have a close relationship as in cervical cancers. It is a disease of advanced life but has been observed as early as the twenty-sixth year. Rhode analyzed the ages of 130 cases and found nearly all between the thirtieth and sixtieth years. A close relationship to the menopause is not proved, and the old theory that ovarian secretions inhibit the growth during menstrual life is combated by numerous instances which occurred during that period. The cancer has been found in young and old, virgin and parous.

The majority of theories advanced as exciting causes by the older observers centered about trauma. Chief of these is the irritation from pessaries, since a number of cases have been described where pessaries which had been worn continuously for years were found imbedded in carcinomatous tissue. This factor, while real, accounts for very few cases, as is shown by Wille, who collected the list. Yet pessaries are so commonly worn, and so many cases have been seen where they have been retained literally for years in an inflammatory mass, that we are forced to believe that the vagina is relatively immune to such insults; otherwise cancer would more often occur.

This theory of mechanical insult appears to receive some support from the fact that carcinoma has occurred in cases of prolapsed vagina. Yet this list is small. Rhode, in 1897, could collect only 4 cases besides his own, which is all the more interesting because operations for prolapse were rare at that time. Nearly all cases were treated with pessaries. Veit, in 1908, adds only 3 other cases to Rhode's list.

Efforts to link the etiology with chronic inflammations, as repeated gonorrhea and syphilis, have not been successful. The theory of the infectiousness of carcinoma is confirmed by at least one instance of marital infection of wife and husband (Wolowski).

Classification.—Primary growths are usually epithelioma, chiefly of the papillary or cancrroid type. More rarely they are infiltrating. A few adenocarcinomata have been described, originating in preformed vaginal cysts (R. Meyer, Bail and Beyen).

Secondary carcinoma may be either squamous cell epithelioma or adenocarcinoma, depending upon the type of the original tumor.

Location of Growth.—Primary carcinoma is usually found high on the posterior wall near the vaginal portion of the cervix. The ring-type form may occur at a lower level. Rhode gives the location of the growth in 123 cases as follows:

Posterior vaginal wall.....	71
Anterior vaginal wall.....	23
Lateral vaginal wall.....	13
Ring-type encircling vagina.....	16

Primary Growths, Appearance and Form.—The everting type is far the more common. It presents in early cases as a fungating mass which projects slightly above the vaginal tissue. The edges are clearly cut. The growth moves readily in the deeper tissues, but is friable and bleeds readily. Ulceration comes on early and there is secondary infection. The surface sloughs and is replaced by a typical, crater-form, carcinomatous ulcer. The margins extend farther beyond the mucosa than is apparent by inspection. The whole mass is fixed in a stiff, infiltrated base.

The infiltrating type of primary carcinoma is rarely seen. It presents a diffuse infiltration, giving the impression of a dense mass of tiny, firm nodules. The edges are not discrete. Extensions are irregular in shape; occasionally the growth completely encircles the vagina. This type is analogous to the infiltrating cancers of the cervix, where extension into the adjacent tissue is an extremely early process. The circulation of the vagina is so good that slough occurs only as a late process. Superficial excoriations, however, are common. The whole mass is brawny, and from the very start is fixed upon the underlying tissues. The vagina is vascular, and is excoriated by the irritating fetid discharge. Contraction of the surfaces occurs early, and the ring-form, circular type may constrict the vagina so that it scarcely admits a finger. This type of growth shows less tendency to infiltrate deeply than other infiltrating forms of carcinoma.

Histology.—Naturally the primary cancers which originate from the squamous epithelium present the characteristic picture of the squamous epithelioma. The surface epithelium may be somewhat thickened, and may contain necrotic tissues, but the true character of the growth is shown at the margins of the tumor. The interpapillary processes are lengthened, branched and anastomosed, and are seen invading the underlying tissue. The epithelial nests stand out in sharp contrast to the normal epithelium.

The primary adenocarcinomata from vaginal cysts are typical cylindrical-cell carcinomata.

The secondary cancers reproduce the original growth in slightly altered form. Both squamous-cell epithelioma and adenocarcinoma have been described.

Method of Growth.—The fundamental processes of both types of primary cancers are identical. The chief difference is the rapidity with which extensions occur. In the papillary growths, there is a short latent period in which extension is not rapid unless ulceration occurs. On the contrary, the indurating type early invades the adjacent tissues.

Extensions progress very quickly from the mucosa to the depths, since the poorly developed vaginal tissue offers little resistance to the further spread. The cancer progresses by direct extension out under the mucosa to the rectum and broad ligament, and rather rarely to the

bladder. It quickly reaches the cervical tip, often by contact infection, but finally by direct extension. More rarely does it extend down to the vulva.

The lymphatic channels are early invaded, and the pelvic glands become involved. The inguinal glands receive metastasis if the primary growth is in the lower vagina. The broad ligaments become infiltrated, with the result that there is compression and involvement of the ureters. General carcinomatosis occurred only twice in Rhode's series of 130 collected cases.

Complication with Pregnancy.—The growth has frequently been observed as a complication of pregnancy. Rhode collected 12 cases. The mother died in 10 cases (83 per cent) and the child in 7 cases (58 per cent). Only twice was there spontaneous birth. There were 4 cesareans with 2 maternal deaths; 2 inductions of labor with 2 maternal deaths. The disease progresses very rapidly during pregnancy.

Symptoms.—The symptoms at first are slight. Leukorrhea, a thin, watery, irritating discharge is the earliest symptom, and may be of long standing before there is blood. Hemorrhage often follows coitus or straining at stool. Later there is backache, and pain, and usually disturbances of the bladder and bowels. With the compression of the ureters, there is uremia and infection, although a rectovaginal fistula may occur before this develops. Rarely there is a vesicovaginal fistula. Death comes as a rule from cachexia.

Diagnosis.—The diagnosis of cancer is usually easy by palpation, although there may be difficulty in determining whether the growth is primary or secondary. There need be no hesitation in diagnosing a primary growth if there is a large cancerous area in the vault of the vagina with an involvement of the outer surface of the cervix continuous to it, and no evidence of carcinoma elsewhere in the pelvis.

Prognosis.—The prognosis is extremely bad. There are few cases of cures, even after the most extensive operation; and these have been calculated on the three-year freedom from recurrence, which is no longer acceptable to cancer students. The case of Lequeu, which remained cured for ten years, is unique in the literature. Since the operation was a partial removal of the vagina, we must regard the cure as accidental and due to the low malignancy of the tumor. It is generally accepted that a case is hopeless when the glands are involved. There are no cures when the disease was complicated by pregnancy.

SARCOMA OF THE VAGINA

Sarcoma of the vagina may occur at any time of life. The disease is rare, although it has been known since 1850, when Guersant described the first accepted cases of sarcoma botryoids. Kaschewarowa-Rudwena made the first extensive study of the same type of tumor in

1872, the same year in which Spiegelberg reported the first accepted tumor of vaginal sarcoma in the adult. Since then a considerable literature has gradually accumulated, in which, however, there still remains much confusion.

Classification.—All classifications which have thus far been advanced leave much to be desired. Histologically, nearly all varieties of sarcoma have been encountered: myosarcoma, including myofibrosarcoma and rhabdomyosarcoma; fibrosarcoma; and myxosarcoma, presenting as round-celled, spindle-celled, giant-celled, or mixed-celled growths. Tumors of nearly identical histology, however, may vary so tremendously in their clinical features that a histological classification fails for clinical purposes. The converse also is true, since tumors presenting similar gross morphology may vary widely, both in malignancy and in their histological picture.

Some, as Wilms, Steinthal, Kolisko, and others, have claimed that because sarcoma is essentially a disease of youth, we should distinguish clearly between vaginal sarcoma of infancy and sarcoma in the adult vagina. The arguments are chiefly based on the histogenesis. They reason that sarcoma in childhood develops from congenital anlage—from displaced embryonal, non-differentiated mesodermal cells; that it is in reality a mixed tumor, since it frequently suggests the teratoma. On the contrary, sarcoma in the adult is purely a sarcoma and results from metaplasia of connective tissue cells. In this way, they account for the presence of the cross-striated muscle fibers in the sarcoma of childhood which are not found in those of adult life. Others, as Pick, while not believing that a distinction between sarcoma of infancy and adult life can be made upon pathogenic and morphologic grounds, agree that the clinical distinctions warrant the separation. Consequently, the majority of authors present this chapter under the headings of sarcoma in infancy, and sarcoma of the adult. Further subdivision does not seem necessary.

SARCOMA IN INFANCY

There are comparatively few recorded cases. Veit, in 1908, states that there were more than 40. McFarland, in 1911, after a critical, painstaking review, tabulates 44 as finally proved. Of these, 34 were sarcoma botryoids, all in children of five years and under; 10 were sarcomata of miscellaneous types, seen in children under thirty-one months of age. The list is not large, since Himmelstrup in 1918 could find but 33 primary racemose sarcomata. The rarity of the disease is well shown by McFarland's tables, which show that sarcoma botryoids has been reported on the average of 1 case every year and eight months. There has been only 1 case (unreported) in our clinic at the University of California during the last 4,000 cases.

Etiology.—Besides the fact that the disease may develop in intra-uterine life, nothing is actually known. Kolisko and Hauser feel that the etiology is best explained by Cohnheim's theory of embryonal vestiges, but many disagree. Trauma does not appear to be a factor.

Age.—At least 1 case has been observed in a newborn child. Textbooks usually state that nearly all cases develop during the first year, but this is not confirmed by the literature from which we obtain the following:

AGE INCIDENCE FOR CASES OF SARCOMA OF THE VAGINA IN INFANCY

First year.....	12
Second year.....	14
Third year.....	12
Fourth year.....	4
Fifth year.....	2

Some claim that the disease may be present at birth but escapes recognition because it is hidden in the vagina. They urge, moreover, that it may remain latent for a considerable length of time, and not develop symptoms, until shortly before it has started to grow sufficiently to form a tumor mass, so large that it can remain no longer in the vagina. They cite in support of this view the case of Demme-Granischer, in which a pea-sized nodule was noticed at birth that did not grow to any extent until the sixth year.

Point of Origin.—All agree that the tumor begins in the submucosa, although there is no agreement as to the exact point of origin. Ahlfeld, who believed that all the sarcoma botryoids are congenital, held that they developed in the papillae which are so numerous in the vaginal wall of the fifth month of intra-uterine life. Pfannenstiel, and many others, considered that they arise from the peri-endothelial tissues of the blood and lymph capillaries.

Location.—The growth usually develops primarily on the anterior wall. McFarland gives the following table showing the anatomical origin of the 34 cases of sarcoma botryoids vaginae which he collected.

Vulvovaginal entrance.....	2
Whole vagina.....	2
Anterior wall.....	10
Posterior wall.....	4
Right wall.....	2
Left wall.....	4
Not stated.....	10

Appearance and Form.—The tumors are essentially polypoid and usually arise from a broad base as single growths. Occasionally, single tumors become ulcerated, and slough spontaneously, and are followed by a diffuse infiltration of the whole vagina. The affected area in such cases usually appears as an infiltrating mass of small nodules. These cases are rare.

The typical form of vaginal sarcoma of infancy is usually described as sarcoma botryoids, or grapelike sarcoma, because the polyps sug-

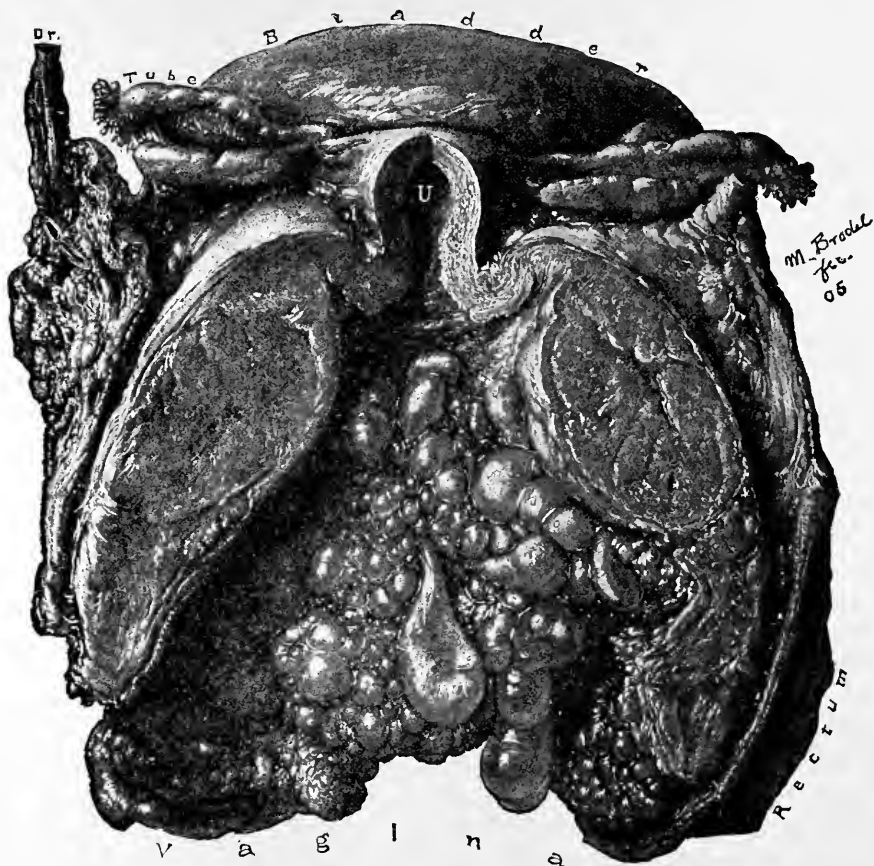


FIG. 21.—SARCOMA BOTRYOIDS IN CHILD (Kelly, Operative Gynecology).

gest numbers of small grapes or currants; or as myxosarcoma (Fig. 21). As the name implies, the growth is characterized by the development of racemose clusters of pedunculated polyps, that are so translucent they appear to be vesicles. The primary color is pinkish gray, but the polyps are usually so hemorrhagic that they look dark red. At the base of the larger polyps are smaller ones in between which the larger growths project into the vaginal cavity. The surfaces of the individual polyps are smooth, since they are covered by vaginal epi-

thelium. At first sight, the early growths suggest a mass of ordinary mucous polyps which are unusually edematous.

Method of Growth.—The tumor first presents as a small, rounded, broad-based polyp, which soon becomes pedunculated and edematous. Similar growths appear in close proximity and presently a lobulate polyp mass fills the vaginal canal, distends the vagina, and is shortly extruded beyond the vulva.

The tumor grows by direct extension, and does not give rise to general metastases. It is purely a local progressively extending tumor. As the tumor grows, its base becomes broader and infiltrates the vaginal wall. Since the majority of the tumors are situated on the anterior wall, the bladder is usually invaded fairly early. Intravesical tumors form with the same morphological picture as the primary vaginal tumor. With further extension of growth, the cervix and uterus become infiltrated, the parametrium is invaded, and the vesical ends of the ureters are infiltrated, so that hydro-ureter and hydro-nephrosis often result. Secondarily, the vulva becomes affected, and the inguinal, iliac and lumbar glands may become involved. Growths on the peritoneum were noted in Körner's case. On the contrary, the growth does not cross the rectovaginal septum, even when the tumor arises from the posterior vaginal wall. Only in the case of d'Arcy Power was the rectovaginal septum infiltrated, which Pick believes was due to extension through the blood vessels.

The metastases are only regional, with the exception of the case of Demme which had a metastasis in the left ovary the size of an orange.

Histologic Picture.—The histological picture varies. All the types of sarcoma are represented. In the 34 sarcoma botryoids cases collected by McFarland, the histologic diagnosis was made in 19. Of these, 7 were mixed-cell, 1 round-cell growth, 3 spindle-cell, while 3 each were described merely as myosarcoma and fibrosarcoma; 1 was termed myofibrosarcoma, and 1 myxosarcoma. The growth was designated in 6 of the 10 vaginal sarcoma in infancy not botryoids, 1 each as rhabdomyosarcoma, myosarcoma, myxosarcoma, round-cell sarcoma, perithelioma and endothelioma.

The free surfaces of the vegetations are covered at first with the normal vaginal epithelium which usually presents ulcerated areas in the later stages of the growth. Even in the cases which present considerable superficial necrosis, the squamous vaginal epithelium will be found intact in the folds at the base of the polyps. As a rule, the mucosa is infiltrated with leukocytes, which process may extend to a considerable depth into the tumor. The superficial margins of the polyps are more cellular than the core, where the cells are widely separated, not only from edema, but often because of myxomatous changes. The tumor cells may be round, or spindle-shaped, or both in combination: giant cells have frequently been described. Embryonic striated muscle

bands have been seen in a large number of cases. Piquand states that they correspond to the striated muscle of a three-month embryo. The secondary and metastatic growths present a similar picture.

Symptoms.—Vulvar pain and a bloodstained discharge are usually the first symptoms, although occasionally a polyp projects from the vulva and gives the first sign of the growth. Pain on urination soon follows, when the bladder becomes involved by the growth's extension, or there is cystitis from bacterial invasion. Although the rectum is not directly invaded, there may be difficulty in defecation, possibly because of the pressure the growth exerts in the pelvis, as well as from the general pelvic infiltration. The patients are usually brought early for treatment.

Duration of the Disease.—This varies considerably, yet is usually only a few months. There is one case, however, that of Demme, in which the tumor was observed at birth, but death did not follow until the sixth year.

Diagnosis.—The diagnosis is often difficult, but must be made tentatively whenever a polyp protrudes from the vulva or where there is a bloodstained discharge. If we would hope to cure we must view all suspicious cases as malignant until all other possibilities are excluded, just as we do in cervical cancer. The literature fairly abounds in cases which were proved to be malignant only when the tumor had been incited to a tremendously rapid growth by the removal of a polyp that was thought to be benign. Tissues should not be removed for microscopic examination unless the diagnosis of malignancy can be followed immediately by a radical operation. Difficulties in making a diagnosis are well shown by the Demme-Granischer case, where only a pea-sized polyp protruded from the vulva of a newborn child, which was considered benign because clinically it remained unaltered and without symptoms for six years.

Direct inspection of the vagina is possible even in the newborn child with the use of the Kelly cystoscope. The vagina should be inspected and the rectum palpated before any attempt is made to obtain a specimen for microscopic examination.

Prognosis.—The prognosis, as the matter now stands, is death. Death results from infectious processes ascending from the bladder or uterus to cause pyonephrosis, peritonitis, pyemia or septicemia.

Therapy.—A review of the literature will convince even the most sanguine that no method of therapy has proved of benefit. The only case that the literature records as cured is the case of Schuchardt (credited by Powers and by Veit to Volkmann—but in reality reported by Fricke. The literature fairly abounds in similar instances where the same case is reported in a student's inaugural dissertation, by a pathologist in a monograph, and by the surgeon at a clinical meeting).

A study of this case convinces us that the result was pure luck and due to the low malignancy of the tumor, since truly radical operations have failed to cure other growths of similar size. In the case in question, a polyp developed from the posterior vaginal wall. At the first operation they cut away with the polyp a piece of the vagina the size of a ten-pfennig piece. The growth recurred. Six and a half months after the first operation, the mass was pulled down with forceps and the lower half of the vagina was removed, together with the broad-based tumor. Following this, the child lived without a recurrence for ten years. The most extensive resection is credited to Israel. Holländer removed for diagnostic purposes a polyp the size of a dove's egg which filled the vagina of a nine-months-old baby and had given symptoms of blood on the napkins for two months. Pick made the diagnosis. In spite of a truly radical operation, in which Israel did a parasacral removal of the uterus and vagina, the growth recurred in a few months. There is, of course, a question whether a cure could have been effected had the *diagnosis made by frozen sections at the operating table been followed by immediate removal*.

Theoretically, radium should supplant operation in this field. As yet there are no cases of five-years standing in which radium treatment has been reported. X-ray has been tried without benefit.

SARCOMA OF THE ADULT

Fortunately, this is also a rare disease. Spiegelberg described the first case in 1872. In 1899, Seitz collected 33 cases. McFarland, in 1911, collected 67 cases. Since then Tracy, 1912, added 2 cases and from time to time other isolated cases have appeared in the literature. Graefe, in 1912, reported the fourth case of melanotic vaginal sarcoma of the adult.

Classification.—Two types are noted. The most common form is definitely polypoid and circumscribed (Fig. 22). The other type appears as a dense nodular infiltration. The tumor is rarely melanotic.

Etiology.—The etiology is not known. The theories which have been advanced for sarcoma in general have been suggested for sarcoma in this region. Few believe that the Cohnheim theory is applicable here, except possibly in some of the cases in the very young. Irritation does not seem to be a factor, otherwise the disease would be far more frequent.

Age.—The disease is essentially one of the sexually active life. It may occur in the pregnant. More than three-fourths of the recorded cases are under forty-five years, as is shown by a study of McFarland's tables, rearranged to show the disease by decades.

Total Cases	
14-20 years inclusive.....	9
21-30 " "	7
31-40 " "	14
41-50 " "	6
51-60 " "	1
60 and over.....	2 (one 70 years) (one 82 years)

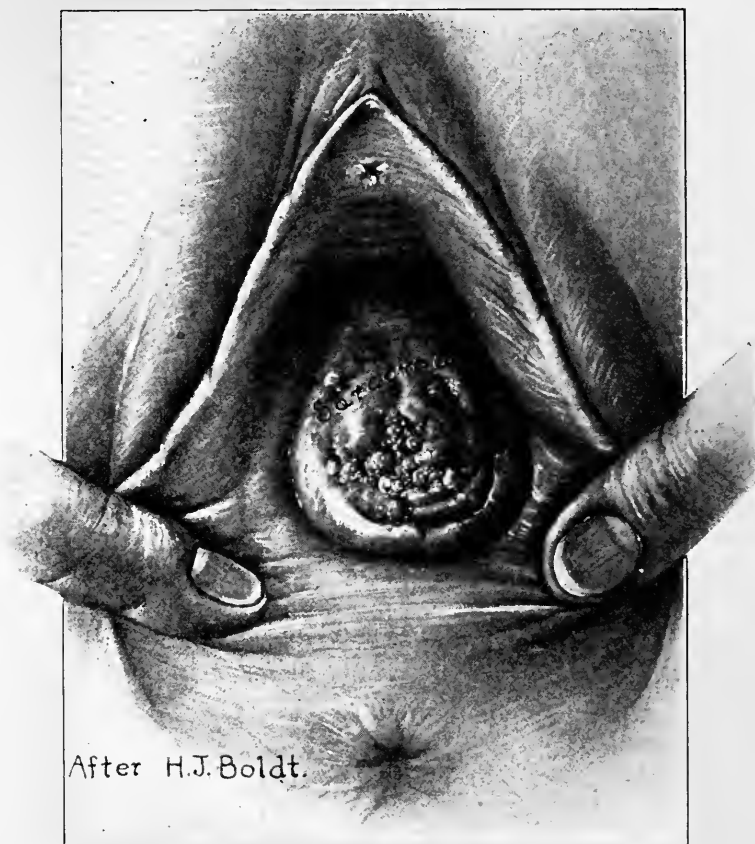


FIG. 22.—VAGINAL SARCOMA (redrawn from Boldt).

Appearance and Form.—The circumscribed type is far the more common, and usually appears as a small, rounded, firm nodule, the size of a bean. It is usually broad-based, but may have a short pedicle. It may develop to considerable size. Jung's first case was a fist-sized polyp. In the early growths, the surface is smooth, since it is covered with intact vaginal epithelium. The growth may be lobulated. Usually hard, it may be soft and edematous. Primarily, it has a pinkish gray color, but more often it is dark red, since it is generally inflamed, although rarely ulcerated.

The infiltrative type is more rare. It usually occurs primarily, but sometimes results following spontaneous necrosis of the small circumscribed type of tumor. This form of growth is nearly always ulcerated, and invariably hemorrhagic. It presents as a mass of soft bossed outgrowths in the infiltrated vascular vaginal wall. Occasionally it encircles the vagina, producing a marked constriction of the lumen.

Location.—The tumor may develop in any part of the vaginal submucosa, yet usually is found in the lower third of the canal. It is equally frequent on the anterior and posterior walls. The location is well shown by McFarland's table which contained, however, 10 cases of vaginal sarcoma in infancy not of the botryoids type.

ANATOMICAL ORIGIN OF SARCOMA VAGINAE CASES NOT INCLUDING
SARCOMA BOTRYOIDS

Vulvovaginal entrance	2
Entire circumference of vagina.....	2
Anterior wall	20
Posterior wall	19
Right wall	2
Left wall	4
Vesicovaginal septum	1
Rectovaginal septum	1
Location not stated.....	17
	—
	68

Histology.—Histologically, the tumors are composed of round, spindle, or mixed round and spindle cells. The spindle-celled form is the most common. The tumor may contain giant cells. There are 4 cases of melanosarcoma on record: Parona, Boldt, Eggel, Graefe. The soft tumors may show a preponderance of myxomatous tissue. Often in the vascular tumors, the spindle-shaped cells may be traced to a proliferation of the endothelium of lymph vessels or capillaries. Some, as Gebhard, have urged that the endothelioma be considered apart from the sarcoma.

The tumors are variously classified as is shown in the following list from McFarland's collected cases:

Spindle-cell sarcoma	12
Round-cell sarcoma	6
Mixed-cell sarcoma	4
(Giant cell included under mixed cell)	
Myosarcoma	2
Myxosarcoma	1
Fibrosarcoma	2
Alveolar spindle cell.....	1
Angio sarcoma	3

Endothelioma	3
Melanotic sarcoma	I
Melanotic spindle cell.....	I
Question as to type.....	II
Type not stated.....	II

58

Method of Growth.—The tumor grows by direct extension and soon reaches the bladder and pelvic connective tissues. The regional lymph glands, inguinal and pelvic, are usually early invaded, although the inguinal glands appeared to be free in both of Jung's cases. The uterus is seldom affected. The rectum, as in the sarcoma of the vagina in infants, appears to escape invasion in the growths which are primary on the posterior wall. It was not involved in Powers' and Seitz's cases, although the growth was extensive, and the rectovaginal wall was infiltrated. It is usually stated that widespread dissemination is rare, yet there are few autopsy records from which we may confirm this statement. Metastases in the lungs, pleura, ribs, skin of chest, axillary and jugular glands were found in the combined cases of Spiegelberg, Bajandi, Herzfeld and von Rosthorn.

Symptoms.—The symptoms are not characteristic and depend upon the nature and type of the growth, its situation, and the extent of the involvement of adjacent structures. In several cases, a "lump" felt by the patient was the first symptom. A foul, bloodstained discharge, backache, a feeling of weight in the vagina and bearing-down pains, dyspareunia, urinary tenesmus, bowel obstruction and anemia constitute the usual list of symptoms.

Diagnosis.—A macroscopic diagnosis is often possible in the circumscribed growths which exhibit evidences of rapid growth, bleed easily and show areas of ulceration. Occasionally, however, they may be confused with the fibromyomata, or with a cyst which has undergone degeneration. There should be little difficulty in recognizing the malignant nature of the infiltrating form, although the differential diagnosis from carcinoma, tuberculous, and luetic ulcers is not easy. The final diagnosis must be made with the microscope. Yet tissue must not be snipped from tumors for diagnostic purposes unless the case is ready for immediate operation. No one may review the original case reports of the literature of pelvic cancers, without becoming firmly convinced that delay in operating following the removal of tissues for diagnostic purposes has lost all chance of cure in many cases. The diagnosis should be made or confirmed by frozen sections only *immediately* preceding operation.

Prognosis.—The prognosis is death, which comes usually from sepsis and cachexia. The disease runs an extremely short course with

an average duration of ten and a half months from the first definite symptom (Seitz, Williams). Contrary to expectation, the course is not more rapid when the disease starts during pregnancy. By the time the symptoms are pronounced, the disease has usually made much headway. Hence patients usually come too late for operation.

Treatment.—Surgery thus far has proved a complete failure, since recurrence has been almost immediate even in supposedly favorable cases. Rubeska's case (1896) of an eleven-years cure stands practically alone, since there are no others cured for the five-year period. Spiegelberg's case was free for four years.

Study of the literature convinces us that there is no hope of surgical cure unless a truly radical operation is done and then only on favorable cases. The entire vagina with the uterus should be removed in one piece by perineal or better by parasacral dissection.

Radium to us seems far preferable to any known method of treatment in spite of the danger of injury to both bladder and rectum. X-ray has been tried often without success. There are as yet no case reports of radium treatment of five-years standing.

In the inoperable cases, the cautery at dull heat may do much to secure relief if radium is not obtainable.

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CHAPTER V

BENIGN TUMORS OF UTERUS AND CERVIX

Fibroids—Definition — Frequency — Age — Etiology — Histogenesis — Growth of uterine fibroids—Classification, histologically, anatomically, clinically—Submucous fibroids—Intramural fibroids—Subserous fibroids—Cervical fibroids—Structure of fibroids—Histology—Blood supply—Lymph supply—Degeneration of fibroids—Frequency—Benign degenerations—Atrophy—Hyaline—Calcareous—Edema and cyst formation—Infection and suppuration—Necrosis of fibroids—Red degeneration—Fatty degeneration—Malignant degenerations, sarcomatous—Relation of uterine fibroids to carcinoma—Effect of fibroids on neighboring and distant organs—Uterus and Adnexa—Tubes and ovaries—Pelvic organs—Cardiovascular changes—Kidney changes—Nerve changes—Symptoms—Hemorrhage—Leukorrhea—Pain—Dysmenorrhea—Pressure symptoms—Diagnosis—Bladder symptoms—Differential diagnosis—Prognosis.

FIBROMYOMA OF THE UTERUS

Definition.—Fibroids of the uterus are benign neoplasms which develop in the wall of the uterus. They are composed of smooth muscle and fibrous tissue in varying proportions, and contain blood-vessels, lymphatics, and probably nerves. The relative proportion of the fibrous and muscle tissue differs greatly. In general, as the tumor grows older, the connective tissues increase at the expense of the muscle cell. The tumors are rarely single and may occur in considerable numbers (Fig. 23). They are usually circumscribed, but may present as diffuse growths. Fibromyomata are also called fibroids, myomata, leiomyomata, and hysteromyomata levicellular. Ordinarily, the terms fibromyomata, fibroids, and myomata are used interchangeably.

Frequency.—Fibromyomata are probably the most common neoplasm in the human body. It is difficult to determine their frequency, since they may not present symptoms and may be diagnosed only accidentally. The majority of textbooks state that they occur in 20 per cent of women over thirty, yet there are few statistics which warrant this figure. Probably the majority of texts quote from the old statistics of Bayle, but to us his statement is not convincing. Bayle says, in 1813, "Car en faisant l'ouverture du cadavre de cent femmes prises indistinctement et agees de plus de trent cinque ans, il est au moins vingt chez lesquelles on trouve un ou plusiere de ces corps, accidentels." Klob later writes that they are present in 40 per cent of all women over fifty. Cullen noted the presence of fibroids in 148 of 742 women twenty years or over who were autopsied at the Johns

Hopkins Hospital between 1889 and 1906, or in 20 per cent of cases. Of the 148 patients, 43 were white and 105 were black. In this series, 33.7 per cent of all the black women twenty years of age or more coming to autopsy had fibroids of varying size, while only 10 per cent of the white patients presented these growths. Other autopsy figures give much lower percentage. In the records of 1860 autopsies made at St. Bartholomew's Hospital in London, Champney found fibroids in 8 per cent of the women. Young and Williams noted them in $7\frac{1}{8}$ per cent of 363 women under thirty-five years autopsied at the Boston City Hospital. The older autopsy records are of interest since, at the

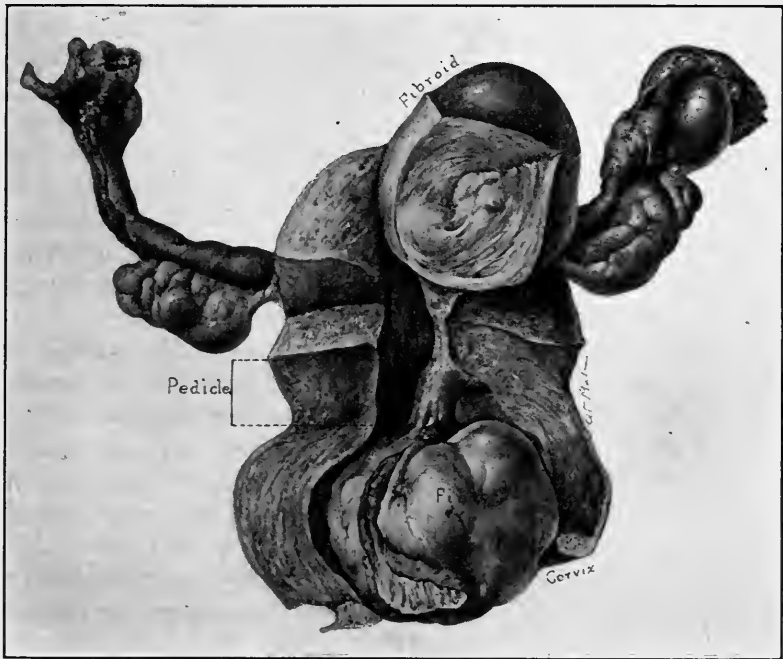


FIG. 23.—PEDUNCULATED AND SESSILE FIBROID.

time of the following reports, operations for fibroids were most uncommon. Pickard, in 1813, found fibroids in 1 per cent of 800 women at autopsy; Pollack, in 1852, found the same growths in 7 per cent of 583 post mortem cases; Braune, Chiari, and West each noted 1 per cent. They are usually said to constitute about 8 per cent of gynecologic cases. Haultain found them in 8 per cent of 2,230 gynecological cases in the Edinburgh Royal Infirmary. Herman reports that $7\frac{1}{2}$ per cent of his women patients over thirty-five were afflicted by the growths; Goetze, 8 per cent fibroids in his gynecologic cases in Greisswald; Doederlein, 8 per cent of cases in Tübingen; while Essen-Moeller, Kleinwächter, and Hofmeier found averages between 4 per cent and 5 per cent. Young and Williams found small fibroids recog-

nizable only after the abdomen was opened at operation in $2\frac{3}{4}$ per cent of 1,402 cases in Boston.

Age.—Fibroids may occur at any period of life, but are usually found during the latter part of the reproductive period. The great majority develop between the ages of twenty-five and forty. They are rarely found in women under twenty-five, yet may occur before puberty. Pick and Anspach have found them in newborn children. Sasaki observed multiple fibroids in a child of nine years. Gusserow reported cases in children of ten, fourteen, and sixteen, 3 cases at eighteen, and 8 at nineteen. Tillaux saw 1 in a nineteen-year-old girl who had been having symptoms for six years. They are rare after the menopause. In Cullen's series of 1,307 cases, the youngest was nineteen; 26 were under twenty-five years; and 44 were more than fifty-five years. More cases were seen at the fortieth year (93) than at any other age.

Etiology.—Little is definitely known regarding the etiology. A perfect host of theories has been advanced to explain their origin; the muscle cells, connective tissue cells, the walls of the blood vessels, and misplaced embryonic cells, all have been credited with furnishing the nidus for their growth. The factors which lead to the development of the tumor are also uncertain.

Numerous examples have been cited which seem to show that *heredity* plays some part in their causation. Occasionally, fibroids are noted in the same family. Yet the majority of these observations must be regarded more as coincidence than as cause and effect, since a growth which constitutes 8 per cent of gynecologic cases, or which exists in from 10 to 20 per cent of women past middle life, must be found frequently in large families.

Women with *negro blood* seem more likely to have fibroids than Caucasians, suggesting that race may have some bearing on the etiology.

Many have advanced the theory that *ovarian hormones* are a necessary factor for the development of the growth. This theory has not been substantiated. There is no doubt, however, that menstruation has an important bearing upon the development of fibroids, since the vast majority present only during sexual life. Webster claims that they do not develop anew in castrated women or after the menopause.

Histogenesis.—The histogeny of these growths is likewise uncertain. Few longer believe Virchow's theory that they develop from uterine muscle cells. Cohnheim's theory of embryonic rests has been applied to fibroids and is supported by many pathologists. Many surgeons recognize a similarity between adenomata of the thyroid and fibroids of the uterus and consider that both develop from embryonic rests. Opitz held that fibroids arise not from muscle fibers but from connective tissue by a process of metaplasia, and claims to have traced the development of small fibroids which started from connective tissue,

passed into muscle tissue, and then to microscopic tumors. He based his theory on the fact that embryologically both the uterine muscle and connective tissue develop from the same undifferentiated process of the mesenchyme, and that later in life this property of metaplasia is again assumed with the result of the formation of fibroids from undifferentiated cells. Roesger first directed attention to the possibility that fibroids develop from the blood vessel wall. Because of the absence of the adventitia in the smaller arteries of small fibroids, he concluded that they must originate in the muscle bands of the arterial wall. Gottschalk thought that the very tortuous portions of small arteries were the site of origin, and that the corkscrew-like capillary arrangement constituted the nucleus about which they grew. Kleinwächter thought he could recognize obliterated capillaries in the wall which separate fibroids from the normal uterine tissue. He also believed that the tumor developed about the blood vessels. Pilliet thought that the adventitia gave rise to embryonic cells which developed into the neoplasm. Many others, however, have rejected all these theories. Cullen, after a careful study of an extremely large series of fibroids, could not obtain any confirmation for the blood-vessel theory.

Leguen, Marien, and Gottschalk believed that inflammation is a necessary factor for the development of the growth. Von Recklinghausen thought that they arose from wolffian remnants; others laid their origin to aberrant müllerian tissue. Theilhaber thought that fibroids were closely connected with disturbances of metabolism and chronic uterine hyperemia.

There is considerable discussion as to the factors which predispose to the growth of the tumor. Sterility is about the only cause which is admitted, although this is denied by many. Those who advocate this theory state that uterine muscle is designed by nature so that it will hypertrophy to meet the needs of pregnancy. In case pregnancy does not occur, it may respond to lesser sexual stimuli, and hypertrophy in a pathological manner with the production of fibroids. Yet the relation of sterility and fibroids is a subject in the greatest confusion, and statistics concerning it must be cautiously studied. The theory just advanced leaves unexplained fibroids in children, and the great numbers of women who have fibroids after having borne several children.

Growth of Uterine Fibroids.—We are ignorant of the factors which are concerned with the growth of the tumors. As a rule, they grow slowly and steadily, and the more fibrous tissue in the tumor, the slower its growth. Consequently, myomata should develop more quickly than fibromata, which is not always the case. There are few statistics which may be used to show the rate at which fibroids develop, since this requires long periods of observation, and the very great majority of tumors are now removed shortly after diagnosis. At a time when operations were not common, Schorler followed 18 cases

in Schroeder's clinic for a long period. He claimed that fibroids grow very slowly; that a tumor three months old is not large enough to be recognized by a bimanual examination; that it takes five years to attain to the size of a man's fist; at the end of 13 years, it may be as large as an adult head. Kleinwächter, as a result of his study of 40 cases, concluded that Schorler was dealing with tumors of unusually slow growth, since in his experience they develop much more rapidly. This coincides with our observations, since we have frequently seen tumors attain considerable size in a comparatively few years. The tumors develop rapidly during pregnancy, and often decrease greatly during the puerperium. One case under our observation shrank from the size of a fetal head at time of labor to a walnut-size tumor three months later. Such cases are not the rule, however. The rapid increase in the size of fibroids during pregnancy is often due to edema rather than to actual hypertrophy, although pure fibroids may occasionally show actual hypertrophy of the individual muscle cells. Usually there is marked decrease in size following the menopause, which fact forms the basis of expectant treatment. Occasionally, however, the reverse is true, and tumors may grow rapidly during this period. Spontaneous disappearance of a fibroid is rare, either in the involution of the puerperium or at the menopause. Only tumors composed chiefly of muscle or containing much edema are likely to show much shrinkage in size. These findings agree with the results obtained in the treatment of uterine fibroma by X-ray, since the growth rarely disappears after the ovarian function is destroyed. The same point has been emphasized by Cullen, who found that only one tumor in twelve disappeared when the tumor was left, and only the ovaries were removed at operation. There was, however, one tumor that grew so much after the ovaries were removed that it finally had to be taken out at a subsequent operation.

Sudden increase of size usually results from edema from some disturbance of the local circulation. Especially is it noticed in certain degenerative processes. Fibroids rarely vary during menstruation, except in the adenomyomata which are then congested and swollen.

Fibroids are usually small but may attain tremendous size. The larger tumors are usually cystic. The largest tumors of which we have record are: Stockard's case of 135-pound tumor in a negress, and Hunter's case of 140-pound tumor, the patient after the operation weighing ninety-five pounds.

Classification.—Fibroids may be classed from several standpoints.

Histologically, they are grouped according to the predominant tissue in their composition. Thus, on the one hand, we have fibroids which are composed chiefly of fibrous connective tissue; on the other, myoma which are chiefly of muscle; properly speaking, fibromyomata lie in between the two. Practically, however, this classification is not observed by the clini-

cian, and the terms "myoma," "fibromyoma," and "fibroid" are used interchangeably. The growths containing glandular tissue are termed adenomyomata.

Anatomically, fibroids may be divided into corporeal, cervical, and intraligamentary. The former is the most common.

Clinically, they are classified according to their position in the uterine wall. Thus we have submucous fibroids, interstitial or intramural, and subserous tumors. The intramural growths are the most common and the majority are said to lie in the posterior wall. All fibroids in the beginning are interstitial, since they develop in the uterine wall. They may develop, however, in any part of the wall, immediately under the stroma or endometrium, or in any level in between. Thus they may long remain in the body of the uterine wall, or may be forced out early toward the plane of least resistance. The tumors which grow toward the uterine cavity finally become submucous; those which start toward the peritoneal surface become subserous or, in case they grow at a uterine level which is not covered by peritoneum, as at the uterine attachment of the broad ligament, they are termed intraligamentous. The tumors gradually pass through the stages in which they are entirely contained in the uterine body wall, come to present on a free uterine surface by a broad base (sessile), and finally their body leaves the uterus and becomes pedunculated. Very rarely submucous, pedunculated growths are forced out from the uterine cavity and break away and escape from the body. In the same way, pedunculated growths on the peritoneal aspect of the uterus may become detached from the uterus, as a result of torsion, etc.; but since they cannot leave the abdomen, they either lie free or become bound up in adhesions which later become vascularized. These tumors are termed parasitic, since they receive their blood supply from other organs than the uterus. We shall follow the clinical classification in our study.

Submucous Fibroids.—Submucous fibroids result from centrifugal development of growths originally interstitial. There may be only one nodule, or the cavity may be fairly studded with tumors, so that it becomes dilated and distorted and the growths are faceted from pressure. Small fibroids a centimeter or two in diameter usually are sessile. The larger tumors act as irritants, and the uterus strives to expel them by muscular contraction. Thus they are forced out until they become pedunculated and grow down in the direction of the cervical canal. They may present at the vagina as a fibroid polyp. The pedicle is usually thin and attenuated. It may, however, be fairly broad. The larger growths are pear-shaped, since they are molded by the uterine pressure. They vary in size from a cherry-stone to that of a six-months pregnancy. Polypoid fibroids may present at the external os during menstruation and recede later, when they are termed intermittent polyps. The growths may be expelled sponta-

neously as a result of necrosis of their pedicle, which is a frequent incident in pregnancy, or following various degenerations of the tumor. Pedunculated submucous fibroids are especially liable to gangrene or putrefaction. They are very important clinically, since they usually lead to alarming hemorrhage. A partial or complete inversion of the uterus may follow the expulsion of the submucous fibroid (Fig. 24), since the thin muscular wall around the base of the tumor is likely to become paralyzed, and follow the tumor as it prolapses. The mucosa

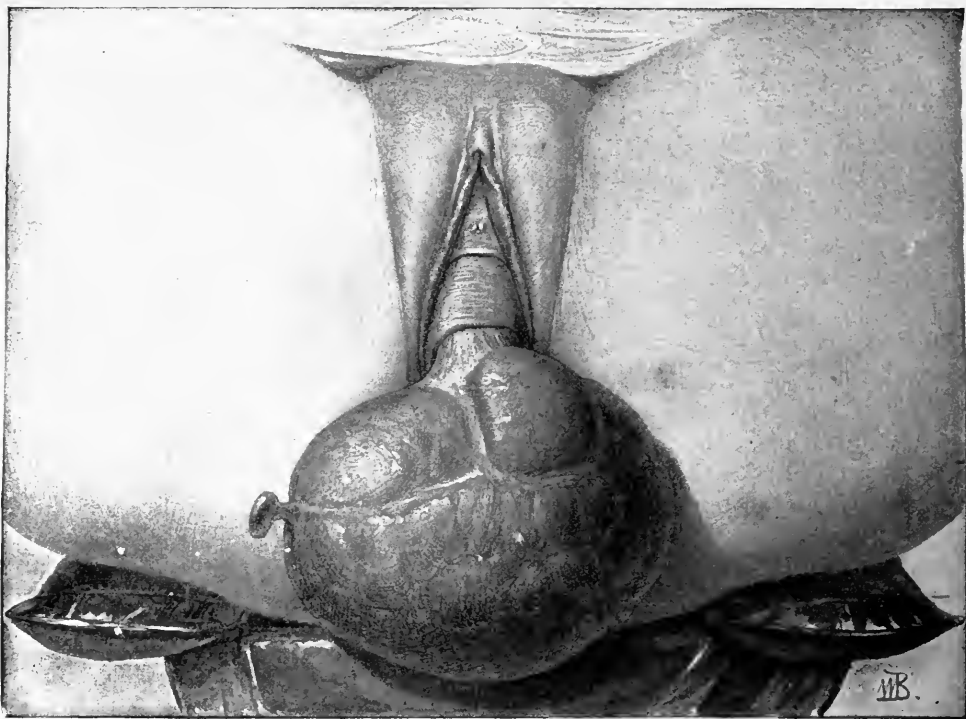


FIG. 24.—PEDUNCULATED SUBMUCOUS FIBROID WITH PARTIAL INVERSION OF UTERUS
(Kelly, Operative Gynecology).

surrounding the tumor is generally hypertrophied and injected; overlying the tumor itself it is usually atrophic. The blood supply is better than that of the other types and, therefore, the tumor grows fairly rapidly.

Intramural Fibroids.—These growths remain localized in the uterine wall and influence the size and shape of the uterus to a very considerable degree. A single fibroid may grow uniformly in all directions and may cause a symmetrical enlargement of the uterus which may readily be confounded with pregnancy (Fig. 25). Usually, however, they develop asymmetrically. The cavity is usually distorted and elongated, but the lining mucosa usually is not much disturbed by the

smaller tumors. The intramural fibroids lie in a thin capsule of loose connective tissue from which they may be shelled out with ease. The only apparent connection between the tumor and its host is a number of small blood vessels which supply the tumor with its nourishment. The tumors are single or multiple; when the latter, they grow at unequal rates of speed.

Subserous Fibroids.—These tumors arise in the body of the uterus and grow outward, and, taking the line of least resistance, push their

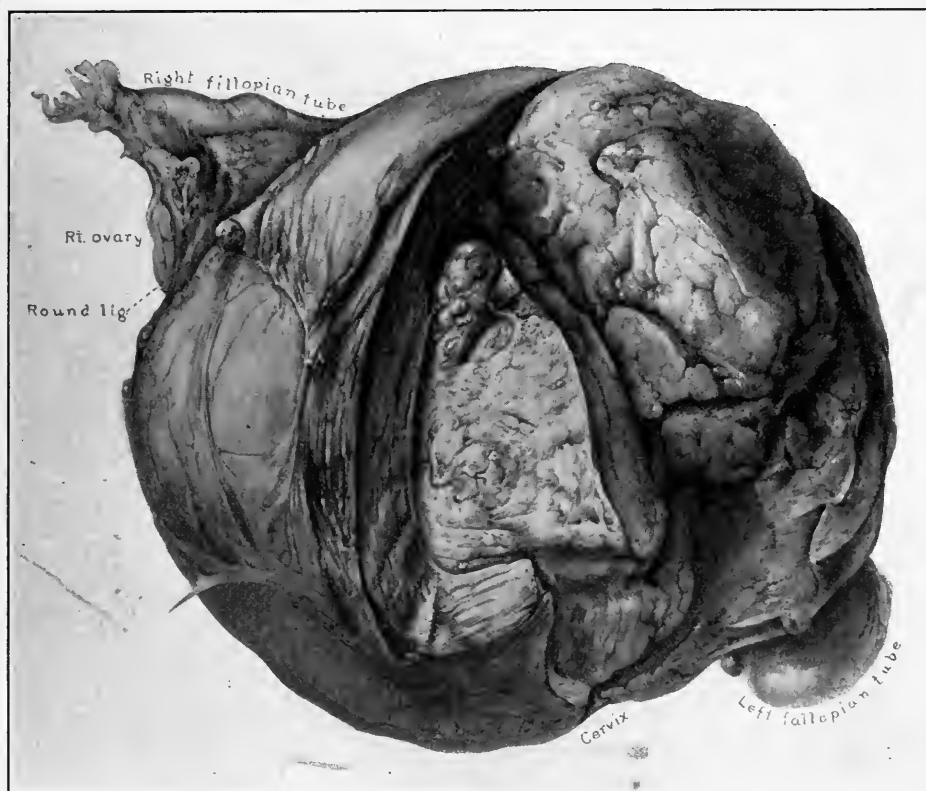


FIG. 25.—SOFT SYMMETRICAL FIBROID SIMULATING SIX MONTHS PREGNANCY. Irregularities in consistency of tumor suggested fetal small parts.

way toward the peritoneal coat of the uterus, carrying a thin layer of muscle stratum before them. This layer of muscle later may give way and finally disappear, leaving the growth covered with peritoneum. At the beginning, they are sessile, with a broad attachment to the uterus, and are partly imbedded in a vascular capsule. Such growths are partly subserous and partly retroperitoneal. If growth continues, the fibroid becomes extruded and the uterine attachment is reduced to a definite stalk or pedicle. The length of the pedicle varies considerably as does its thickness; the broad pedicles contain muscle, connective tissue, and blood vessels; the thinnest pedicles contain only

blood vessels covered with peritoneum. The thickness of the pedicles influences the character of the growth, since they grow directly outward from a firm base, or are deflected by the pressure of other abdominal viscera when the pedicles are thin. Pedunculated subserous fibroids may acquire a great freedom of movement which may lead to strangulation of the growth with serious consequences. Complete separation from the uterus not infrequently occurs, when the nourishment of the tumor is obtained by adhesions to omentum, etc., by the formation of a circulatory anastomosis. These growths very rarely lie entirely free in the abdomen. Subserous fibromata are usually multiple and of small size, yet occasionally they attain considerable dimensions. Spencer Wells describes one that weighed thirty-four pounds. The peritoneal coat is firmly attached to the tumor. Subserous fibromata may be lobulated or smooth. They frequently have large blood vessels on their surface which may rupture from trauma, giving rise to profuse intraperitoneal hemorrhage. Adhesions to surrounding structures are common, with resulting disturbances of function. When the intestines become adherent to a growth which has broken down in this manner, infection may pass through from the bowel.

Various complications arise from injury to the pedicle. Torsion is common, although much less frequent than in ovarian tumors. The resulting changes vary according to the number of turns the tumor makes, the tightness of the twist, and the suddenness with which torsion is accomplished. Sometimes the uterus itself is the seat of the torsion, especially when it has been thinned by the traction caused by the upward growth of the tumor so that it has become in effect the pedicle of the tumor. Torsion of 120 degrees or more is frequently noted, and Lenander has described a case in which the tumor and uterus were thus finally separated from the cervix.

In the milder forms, congestion and edema result from the disturbance of the circulation, and the tumor may even be distended with blood. The arteries are less liable to compression because of the support given by the thickness of the wall. Occasionally the blood vessels of the pedicle become thrombosed in the later stages of torsion.

Cervical Fibroids.—Cervical fibroids are usually stated to be rare and to constitute only 5 per cent of uterine fibroids. Schroeder and Lee described them in 8 per cent and 15.5 per cent respectively. Courty found them in 16 per cent of 131 cases of fibroids.

They arise most often from the posterior cervical wall and may be subvesical, retroperitoneal or intraligamentary, according as they project under the bladder, under the peritoneal investment of the lower uterus, or out into the broad ligament (Figs. 26, 27). Haultain classifies them according to their vertical position as supravaginal, intravaginal and intervaginal. Like uterine fibroids, they may remain localized to the body of the cervix when they are termed interstitial; or

they may extend to the cervical cavity when they are submucous. Subserous cervical fibroids, strictly speaking, do not occur, since the cervix is situated at some distance from the peritoneum. Yet outgrowths from the cervix may burrow into the subserous connective tissue, when they are more or less analogous to subserous uterine fibroids.

Cervical fibroids usually cause clinical symptoms, varying according to their size and location. They do not have the same latitude of growth as do fibroids of the uterine body, and pressure symptoms come



FIG. 26.—CERVICAL FIBROID. Note lengthening of cervical canal, and Nabothian follicles.

comparatively early. When the interstitial growths attain considerable size, the body of the uterus is carried upward, and finally comes to ride upon the egg-shaped tumor very much as does the adrenal on the kidney. On bimanual examination the uterine body may be confounded with a subperitoneal fibroid. The cervical canal is usually greatly altered. It may be elongated to five or six inches in length and is expanded laterally. The external os is changed in shape, and may present either as a crescent, or crack, or may be completely opened up by a submucous growth. The os may be pulled high up under the symphysis, or in one of the lateral fornices. The tumor may block the pelvis and completely obliterate the cervical canal and vaginal

fornices. Frequently the urethra is crowded downwards; at times, however, it is pulled upwards by the displacement of the bladder wall. Urinary symptoms are common with this tumor.

Submucous cervical fibroids may remain sessile, or may become pedunculated and appear as myomatous polypi at the external os. These latter may become necrotic and present as a sloughing mass in the vagina. The expulsion of the polyp through the external os may

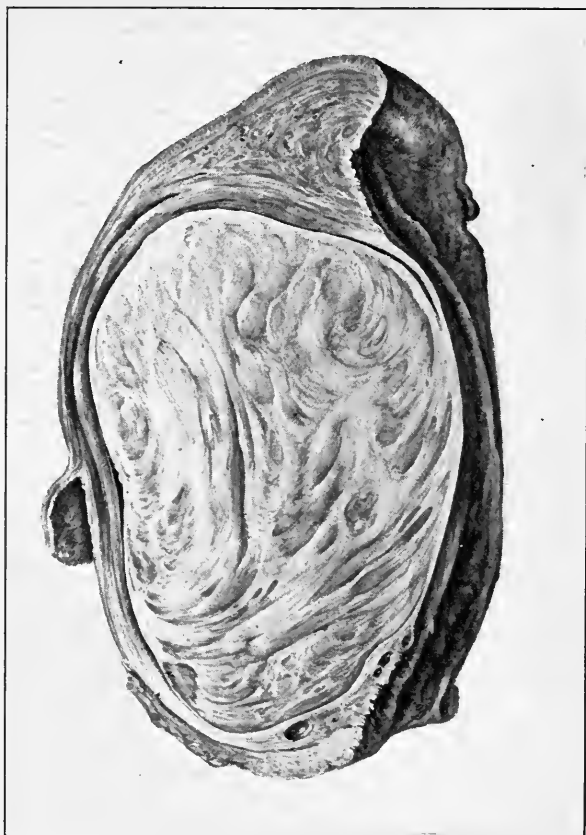


FIG. 27.—CERVICAL FIBROID. Sagittal section of Fig. 26.

be accompanied by painful contractions. The tumors do not, as a rule, attain a large size.

Fibroids which arise from the superficial muscle tissue of the cervix and grow outward into the surrounding cellular tissue are uncommon. They may grow to a considerable size and burrow between the broad ligament, when they are of clinical significance, both on account of their displacing the ureters and uterine vessels and because their removal may be attended with unusual difficulty. When the growth becomes localized on the posterior wall, the pouch of Douglas is distorted and the sigmoid and rectum are usually elevated. When the

growth is situated on the anterior vaginal wall, the uterovesical peritoneum and bladder are raised.

Cervical fibroids are said to grow more rapidly than uterine fibroids on account of their proximity to the uterine vessels. Alteration of menstruation is not common unless the uterus is enlarged.

Structure of Uterine Fibromyoma.—Fibroids are of the same structure as the uterine wall, namely, muscle and connective tissue. The muscle is arranged in longitudinal and transverse bundles bound together by the connective tissue. The bundles are not arranged in regular order. In the smaller tumors, they present as irregular interlacing masses of unequal size, while in the larger growths they are arranged in whorls. The blood vessels are comparatively few, although very rarely one finds a fibroid containing many large dilated blood sinuses, a true telangiectatic fibroid. Surrounding the whole tumor is a zone of connective tissue which is arranged as a capsule, and which sharply separates it from the uterine musculature. The capsule is pierced by the small nutrient blood vessels which run from the uterine musculature into the center of the whorls, and appear to the naked eye as the only connective bands between the uterus and the tumor.

The appearance of the uterine musculature varies considerably according to the location of the tumor. The larger intramural growths are covered with hypertrophied muscle cells which resemble those in pregnancy; while surmounting the pedunculated types, which have escaped from the body of the uterus, the uterine muscle may be so thin and filmy that it is not recognizable. On section, the fibroids give a sense of almost cartilaginous hardness, and the peripheries of the mass retract so that the cut surface is bulging. The surface presents a dull white, glistening structure, broken by darker areas which constitute the outlines of definite whorls. The capsule retracts with the margins of the tumor and presents in contrast dark red in color, from the blood which has escaped in its meshes.

Histology.—The smallest fibroids are composed exclusively of smooth muscle cells; when they obtain a diameter of 1 centimeter, fibrous tissue can be seen. Microscopically, fibroids have no definite capsule; and the identity of the new growth can be made out by the condensation of the muscle cells and their nuclei, which stain deeper than the surrounding connective tissue elements. The muscle cells are spindle-shaped with long, narrow nuclei; on transverse section the central round nucleus is surrounded by a spherical mass of protoplasm. Mallory, in appropriately stained material, was able to demonstrate neuroglia, myoglia and fibroglia in the various tumors. Speaking of myoglia, he says that "while in general the smooth muscle cells closely resemble those found in normal tissue, they may vary considerably from the normal type; the cells may be long and thin and the nuclei the slenderest of rods; in other cases the cells are short and

thick with short oval nuclei." The variation in shape depends upon the rapidity of growth of the tumors. The slowest growing fibers are the most slender. As the fibroid grows, it usually acquires a capsule, that is, becomes more and more distinct from the muscle tissues of the uterine wall, and comes to lie in a loose cellular connective tissue bed, which is characterized by its rich blood and lymph supply. From such minute origin, fibroids may develop even to the enormous size of Hunter's 140-pound tumor.

Blood Supply.—Sampson in 1912 studied the blood supply of one hundred fibromatous uteri injected immediately after operation with substances impervious to the X-ray. He believes that the nutrient arteries of the tumors spring from radial or peripheral branches of the uterine arcuate arteries. They pierce the capsule of the tumor, and immediately divide, into either a diffuse proliferation which penetrates the entire tumor, or into a series of arterial trees. There are usually only one or two chief nutrient vessels, although in the larger growths there is a secondary nutrient system. The latter consists of an anastomosis of a number of arteries in the uterus surrounding the tumor, and of similar vessels in the periphery of the fibroid. The nutrient artery is the main supply, and follows the tumor as it moves in the uterine wall. The secondary system may be temporary, or a secondary development, resembling the blood supply which springs from vascularized adhesions about the surface of subserous pedunculated growths.

The investigator was not able to demonstrate the venous system.

Lymph Supply of Fibroids.—Polano, in 1913, studied the lymph supply in sixteen fibroids similarly injected with a solution of camphor and coloring matter in ether. He showed that the anatomical relation of blood and lymph is very intimate, although there is no definite perivascular lymphatic arrangement. The lymphatic supply differs in single and multiple growths. The one seen in single unicentric nodules shows a broad pedicle, uniting the tumor and surrounding tissue, through which pass a number of lymph channels.

The other type is seen in small conglomerate nodules, which have a number of such broad connective tissue bridges, at various points between the tumor and the capsule, containing numerous lymph channels.

In addition, there is, in both types, a canal system in the fine spider-web type of connective tissue that unites the tumor and the entire length of the capsule.

Degeneration of Fibroids.—There is no tumor which may be associated with a greater variety of pathological processes than a fibroid. Situated in an organ which undergoes so many changes in size and in physiological activity, which becomes functionally inert long before senile changes appear elsewhere in the body, and which at the time of atrophy is subject to a variety of lesions, the growth is under many

influences, and may undergo almost any form of degeneration, and also produce effects on neighboring or distant organs.

Thorough and careful examination of fibroids usually shows some form of degeneration. Largely owing to the disproportion of the size of the fibroids and its blood supply, the tumors are especially liable to degenerative alterations from comparatively slight changes in circulation. These degenerations may be divided broadly into benign and malignant. Many of the benign changes are various stages in the same general pathological process.

FREQUENCY OF.—In attempting to form an estimate as to the frequency of degeneration, the following figures are of interest:

DEGENERATION

Frequency of	CASES	
	Uterine fibroids	Degeneration
Webster.....	210	52
Noble.....	337	62
Scharlieb.....	100	26
Cullingsworth.....	100	52

Noble, in collecting 2,247 cases, found the following proportions of degeneration:

Form of	Number cases	Per Cent
Hyaline.....	72	3.1
Hyaline with calcareous infiltration.....	8	0.3
Calcareous.....	39	1.7
Myxomatous.....	89	3.4
Cystic.....	58	2.5
Hemorrhagic.....	13	0.57
Necrosis.....	119	4.7
Fatty degeneration.....	7	0.25
Edema.....	17	0.74
Sarcoma.....	34	1.4
Carcinoma corpores.....	42	1.8
Carcinoma cervix.....	16	0.7

Deaver as the result of analysis of three hundred and forty-five consecutive operations for fibroids concludes 10 per cent of the cases requiring operative treatment are having symptoms which are largely the result of benign degeneration.

BENIGN DEGENERATIONS.—Benign degenerations are due to many causes, among the most common of which are emboli in the afferent artery, hemorrhage from trauma or twisted pedicle, and alteration in the blood supply incident to menstruation, pregnancy, puerperium and the menopause;

more rarely dislocation of the tumor or injury to the growth during labor may initiate the process.

Under the heading of benign degenerations, we may list atrophy, hyaline degenerations, calcareous changes, edema, cystic and myxomatous degenerations, the various necroses and consequences of inflammation. While these are benign degenerations in contrast to the malignant changes, they may at the same time cause symptoms of alarming character and may actually cause death.

Atrophy.—With the cessation of the menstrual function and the diminution of nourishment which follows the physiological involution of the genital organs at the menopause, fibroids frequently undergo spontaneous atrophy and diminution in size. Marked atrophy frequently ensues as the result of bilateral oöphorectomy, an operation which was frequently performed in the early days of abdominal surgery when the mortality for hysterectomy was in the neighborhood of 25 per cent. Lawson Tait, in 1872, first advocated it and showed its feasibility. Atrophy may come about during the puerperium. X-ray and radium may also produce sclerotic changes. As a result of atrophy, the tumor cells are replaced by new fibrous tissue and frequently there is a marked overgrowth of connective tissue so that the nutrient vessels are constricted. The tumor, as a result of the fibrosis, becomes hard and indurated in character. These changes are most common in pedunculated subperitoneal growths. Atrophy of fibroids does not invariably occur with the onset of the menopause, nor do X-rays or radium always produce permanent atrophy.

Hyaline Degeneration.—This is the most frequent degeneration found in fibroids, and is the first change to occur as the result of malnutrition. In 3.5 per cent of Noble's collected cases and in 11 per cent of Deaver's, there were more or less extensive areas. Practically all tumors, whatever the size or situation, show this change in varying degrees, either histologically or grossly. When the process is very extensive, the center is likely to break down and become necrotic; even a large cystic cavity with irregular, softened walls may result (see cystic changes). The distribution of the hyalin is variable. Frequently the fibrous tissue between the muscle fibers is first attacked and the muscle bundles are preserved intact. When the muscle bundles become involved, the cells are swollen and their outlines are indistinct or lost, so that the protoplasm seems to have fused. The nuclei are fragmented and in some instances have completely disappeared. They are more resistant than the cytoplasm, however, and may remain as the last evidence of the original cell structure. Infrequently the hyaline degeneration appears to begin around the blood vessels, and thence spread to neighboring structures. Usually, however, blood vessels are found lying in homogeneously staining areas where degeneration has completely altered the structure of the surrounding tissues. Hyaline areas are almost devoid of cell structures.

Macroscopically, hyaline areas present a yellowish white appearance,

not unlike areas of fat. The color is due to the blood alteration and old blood pigment from hemorrhage. The areas may be sharply circumscribed, and may occur *en masse* or be scattered throughout the growth. The change may be limited to one nodule, or may present simultaneously in several fibroids. On palpation, the tumor may be firm and may differ in no way from ordinary fibroids. Others are soft and succulent and give the suggestion of lipomata.

Hyaline degeneration is of no clinical significance unless the retrogressive process goes on to liquefaction or cyst formation. Such an occurrence is usually marked by a rapid enlargement of the tumor, and augmentation of the existing symptoms. Sarcomatous alteration may originate in the areas of hyaline changes. The cells which resist the hyaline alteration lie free in the hyaline or serous fluid and appear occasionally to take on active development.

Calcareous Degeneration.—Calcareous deposits are found usually in atrophic and sclerotic areas of tumors which have undergone a profound disturbance in their circulation. They cannot be laid down in living tissues but are found in cells that are dead or which have suffered serious injury. Litten, in 1879, proved that lime salts were deposited in the kidneys of rabbits within a few hours after the renal vessels were tied.

Calcification frequently occurs in fibroids during the climacteric, probably as a result of the circulatory changes and the atrophy which ensues at that time. It is commonly found in subserous pedunculated growths which have become detached as a result of torsion, or in the tumors which hang by a narrow pedicle. It may occur in degenerated areas of interstitial growths, which may have been moved about by the changes coincident with pregnancy. It rarely occurs in submucous growths, probably because they rarely survive in loco profound disturbances of circulation. The deposits consist of phosphates and carbonates of lime which infiltrates the degenerated areas of the tumor. The mass grows in size, forms concentric plaques, and often unites with neighboring infiltrated areas to form definite calcareous nodules. Occasionally, the whole tumor becomes infiltrated with the granular calcareous material, although rarely does it become completely calcified. Pedunculated tumors which have undergone more or less complete calcification may be thrown off into the abdomen or the uterine cavity. They are known as "womb stones." The periphery of the tumor often presents many areas of calcification. If they coalesce, they may completely occlude the blood supply of the tumor and cause necrosis of the central portions. Histologically, the concentric calcareous plaques present a characteristic picture since they are intensely colored by the nuclear stain. In the earlier stages, they are seen as fine granules in the fibrous tissue and muscle cells, which have been partially or completely deprived of their blood supply.

The chemistry of the process was shown by Klatz in 1905. He believes that fatty changes in the degenerated areas precede the deposits of calcium salt. The fatty changes are followed in time by the appearance of soap or a soapy substance which unites with the albumins of the degenerating cell to form soap albumin. Calcium from the blood unites with the soap albumin to form insoluble calcium curds or double calcium soap. The latter, by the action of substances in the body fluid containing carbonic or phosphoric acids, are then decomposed into phosphates or carbonate of lime, and remain as insoluble deposits in the tissues.

Calcified fibroids may cause much trouble even after the menopause. Louis, Noble, Henning and others have collected cases which developed pressure symptoms, some of them blocking the ureters and causing death by uremia, creating fistulae to the bladder, causing torsion and hemorrhage into the peritoneal cavity. Piquand analyzed 81 cases of calcified fibroids and found the following complications:

- 29 cases caused compression on neighboring structures.
- 15 cases caused metrorrhagia.
- 18 cases caused suppuration.

Of 26 deaths not following operation

- 5 resulted from peritonitis.
- 3 resulted from intestinal obstruction.
- 2 resulted from changes following retention of urine.
- 1 resulted from hemorrhage.
- 7 resulted from anemia and cachexia from suppuration.
- 1 resulted from rupture bladder.
- 6 resulted from cancer of uterus in conjunction with calcified myoma.
- 1 resulted from torsion of uterus.

Edema and Cystic Degeneration.—These processes usually affect subserous tumors of large size. They are rarely found in submucous forms and very rarely in the interstitial types. Piquand states that they are seen most often in the larger single growths (Fig. 28).

Edema usually results from interference with the return circulation of the tumor so that there is a passive congestion. The tumor is swollen, smooth, and rounded, and looks congested. The surface is reddish and contains many large, branching, dilated blood vessels. The tumor feels soft and sometimes fluctuant. The edema may be local or may extend throughout the whole tumor. In the early stages, the growth is soft and exudes serous fluid from cut surfaces. In the more advanced forms, one sees a number of homogeneous soft areas which are translucent. A thin,

watery lymph exudes from the cut sections. Small cavity formations may be seen on close inspection (Fig. 29).

Cystic degeneration usually follows extensive hyaline degenerations. It results from the liquefaction of the hyaline areas. The resulting cavities are not lined with endothelium but by hyaline tissues which have not yet undergone liquefaction. The cavities grow by the breaking down of trabeculae which separates neighboring cavities, and by the amalgamation of small cysts. Cystic formation may occur in small areas, or may involve the whole tumor simultaneously. The small cysts which form from the breaking down of trabeculated areas of hyaline degeneration are far more com-

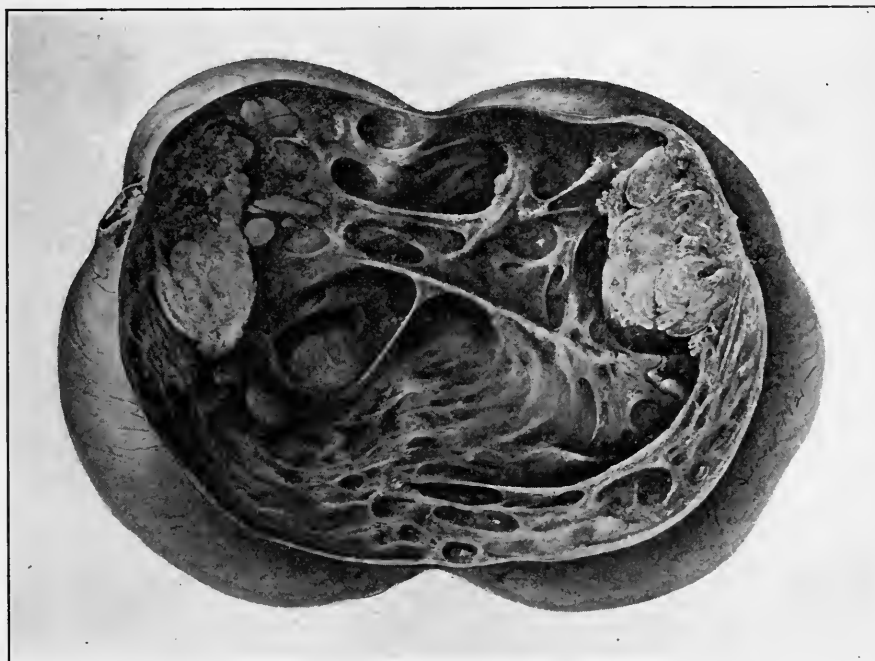


FIG. 28.—LARGE SUBPERITONEAL FIBROID WITH MARKED CYSTIC DEGENERATION.

mon than the massive cysts which have involved the entire tumor. The color of the cysts ranges from yellow to brownish green, or blood color, and is due to blood pigments which have escaped from thrombosed blood vessels. There is no other suggestion of blood in the cyst contents save occasional streaks, and the fluid contains neither leukocytes nor fibrine ferment, nor does it coagulate on standing.

The last stages of liquefaction are frequently termed myxomatous, since they give this appearance to the naked eye. It rarely proves to be true myxoma, however, a point emphasized by Meslay and Heyenne.

Cystic degeneration does not always follow a hyaline change. It may come on after necrobiosis of small or large areas. Cystic spaces lined with endothelium occur in lymphangiectic and telangiectic tumors, which are only

blood and lymph spaces dilated to varying degrees. This type of tumor frequently changes in size from time to time, and the angiomatous form may pulsate synchronously with the heart beat. Cystic degeneration may also occur as the result of radium treatment. The microscopic findings are fairly constant. In the earlier stages, the blood vessels are dilated, and the tissue cells are swollen. The cells do not stain readily and the protoplasm

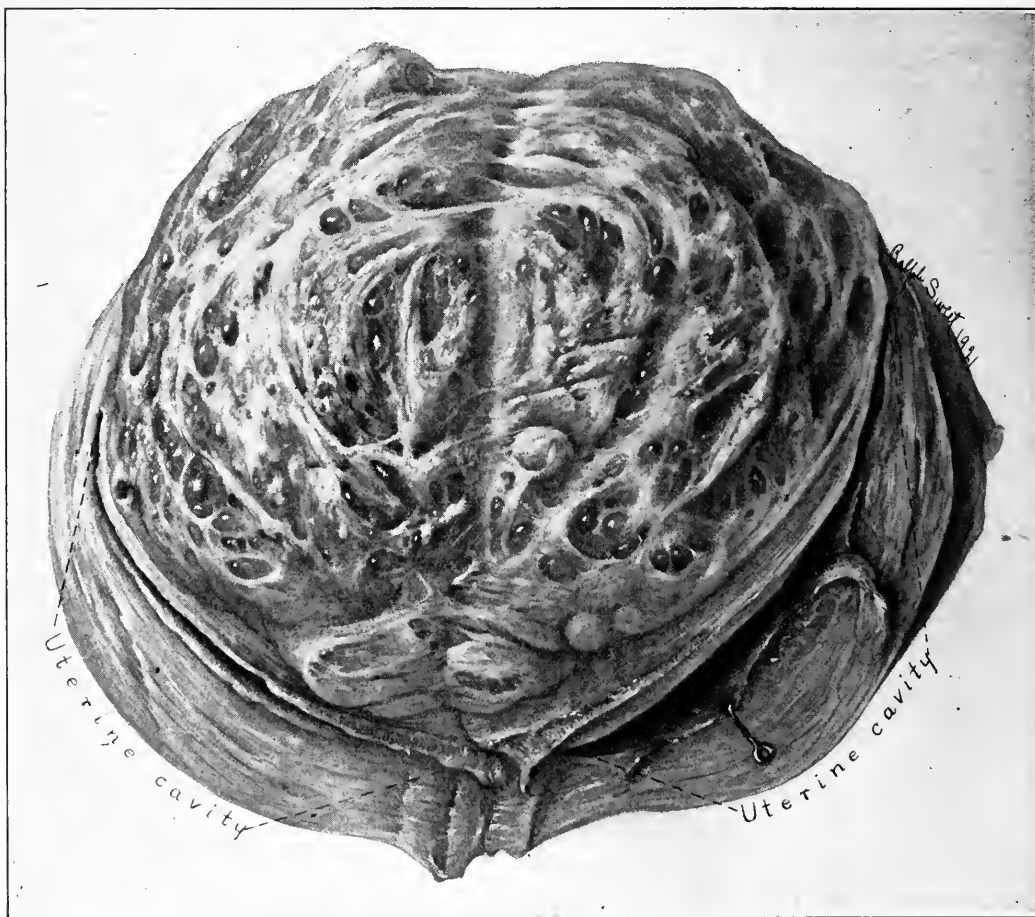


FIG. 29.—SOFT FIBROID WITH CYSTIC DEGENERATION.

is granular. Later, the degeneration has progressed so that there is left only a few cellular fibers, which are separated by the serous exudate, without trace of nuclei. This type resembles myxoma.

INFECTION AND SUPPURATION.—Tumors of low vitality may readily become infected in case they are already the seat of other degenerative processes, and especially if the uterus has undergone some profound disturbance of the circulation, which in turn reacts upon the tumor. The infection may come from one or more sources, and may readily progress to

suppuration. Usually it proceeds upward through the lower genital tract, and into the uterine cavity. Submucous tumors are most apt to become infected after abortion or infectious processes in the puerperium (Fig. 30) The uterine circulation at this time is undergoing the changes characteristic of involution, which undoubtedly tend to favor the progress of bacterial invasion. The same changes are noted frequently after curettage or other intra-uterine manipulations, in which a portal of entry is afforded by the injury to the endometrium or by partial dislodgment of the tumor. Some claim that the continued use of ergot tends to increase the susceptibility to

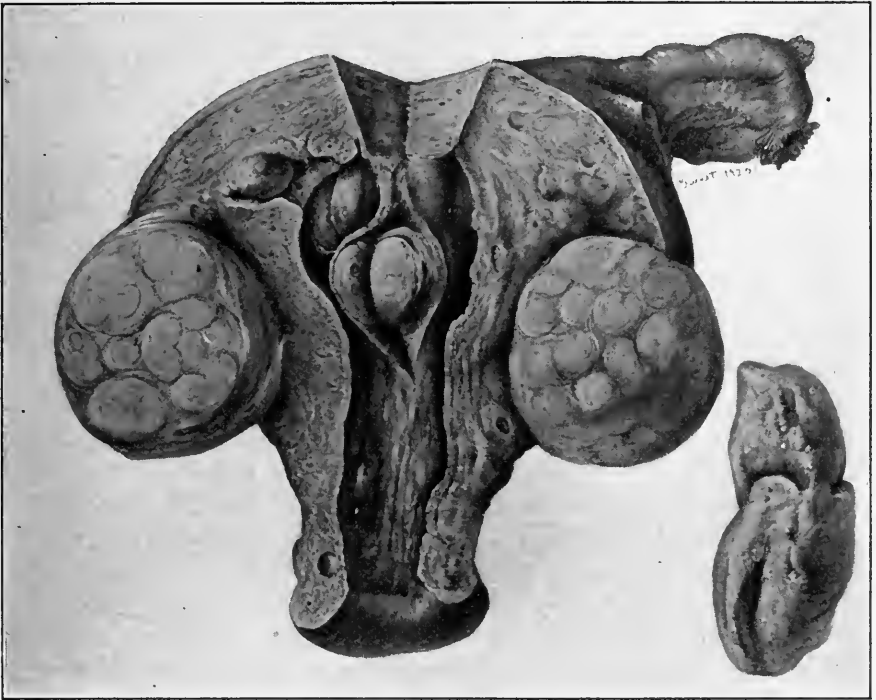


FIG. 30.—MULTIPLE FIBROIDS. Necrotic submucous fibroid expelled after abortion.

infection and, for this reason, they have done much to discourage the routine treatment of submucous tumors by ergot preparations. Many instances have been recorded in which the trauma attending intra-uterine electrical treatments was responsible for the infection. Small intramural tumors may readily become infected shortly after they have become loosened from their bed by the involution following pregnancy. We have seen several cases in which suppurating fibroids have been passed in the second week of a febrile puerperium. All of these cases were known to have many small uterine fibroids during the pregnancy. Cullen reports a case in which tubercle bacilli were found in the necrotic center of an intramural fibroid. Infective agents find access easy to small areas of hyaline or cystic degeneration in

intramural fibroids, when the uterine cavity is infected and the fibroid impinges upon the endometrium.

Subserous fibroids may become infected when they become involved in adhesions with pus tubes, ovarian abscesses or other pelvic inflammatory processes. Areas of former degenerations, and profound disturbances of the local circulation are necessary prerequisites for serious infection of the tumor. Occasionally the infection passes from the bowel to the tumor in such cases as are involved in inflammatory adhesions. The appendix is the chief offender, after which comes the sigmoid and the small bowel in order of frequency.

Intraligamentary tumors may become infected by extension of infection from a tuboovarian abscess which is also adherent to the rectum. The infection may remain localized or may become general. If the process becomes widespread, the symptoms undergo a sudden change with the advent of suppuration.

Various pictures may present with infected fibroids. The local infection may be limited to the interior of the tumor or may break through the capsule, so that the infection extends about it—between it and the matrix of the tumor. As a final result, the tumor may be liberated from its site and expelled from the uterus. Suppurating tumors within the abdomen are usually walled about with omentum and adherent bowel. They may be expelled into the bladder or bowel, yet more commonly slough away and are expelled through the uterine cavity.

Pain, lancinating in character, is noted. There are chills and fever. The patient may have a sallow color and anemia from septic absorption. Kidney damage, as shown by albumin and casts, may be present. If the suppurating fibroid opens into the uterine cavity, there is a profuse, foul-smelling, vaginal discharge. Suppurating fibroids may slough and be expelled through the uterine cavity, into the bladder, bowel, or peritoneal cavity. The advent of this complication greatly increases the risk if operative treatment is necessary, particularly if the patient's resistance has been lowered by a long-continued, suppurative process.

NECROSIS OF FIBROIDS.—Necrosis is frequently present in small or large areas. It is usually preceded by hyaline degeneration as the initial change indicative of faulty nutrition. Necrosis is a terminal condition. It usually affects a limited part of the tumor when it does not necessarily give rise to symptoms. Clinical manifestations invariably follow a widespread necrosis.

Necrosis may occur in any type of tumor. Christopher Martin found it in 4 per cent of his series of fibroids; Noble in 5 per cent of 119 cases; Tracy observed it in 5 per cent. Necrosis often follows torsion of a pedunculated fibroid and is associated with local hemorrhagic or anemic conditions. It occurs in isolated foci in the midst of apparently normal fibroid tissues. The central part of the tumor is usually affected because it is furthest from the blood supply.

The necrotic areas are likely to become infected in submucous tumors

during the puerperium. Gangrene and sloughing may result with the onset of pain, fever, leukocytosis, etc. The color of necrotic fibroids is due to the pigment from blood which becomes laked by the action of lipid substances.

According to Leith Murray, the tint of the tumor varies according to the amount of the lipid substances which are present to produce the laking of blood. Thus we have:

Red degeneration . . . lipid, just sufficient to produce perfect hemolysis.

Brown, black, gray . . . lipid, in moderate excess.

Yellow necrosis . . . lipid, in excess sufficient to bleach.

White necrosis . . . lipid, insufficient to produce hemolysis, the latter being restrained by blood plasma.

RED DEGENERATION.—This has assumed considerable clinical importance since it was described by Gebhard in 1899, and by Fairbairn in 1903. It usually occurs in pregnancy, although it is noted rarely in nonpregnant conditions, but the process is never so well marked and complete. The term “necrobiosis” has often been used erroneously as synonymous with red degeneration. Some employ the term to indicate a partial destruction of tissue in contrast to necrosis, in which there is actual tissue death. The terms cannot be used interchangeably, since red degeneration may terminate in complete recovery and restoration of the lost vitality of the tumor, although usually it goes on to liquefaction and total necrosis. Nécrobiosis is merely a phase in a degenerative alteration. The question of color of the degenerative process is independent of the stage of the alteration and dependent only upon the vascular changes in the neighborhood.

Red degeneration is essentially an aseptic degenerative process which is associated with hemolysis and autolysis of tissue. Only rarely are there invading organisms which come usually through the lower passages. Such a secondary invasion is of grave prognostic significance and fortunately is not common.

Murray believes the process is inaugurated by hemolysis from lipoids, since the lipoids in degenerating fibroids are markedly hemolytic. He states that normally such action is held in check by blood plasma which inhibits hemolysis. When the lipoids are greatly increased in amount, so that they cannot be inactivated, hemolysis results and oxyhemoglobin can be demonstrated by the spectrum. Thrombosis forms from a deposit of fibrin in the blood vessels and the disintegration of the blood corpuscles. The largest thrombi occur in pregnancy and account for the pain, the rapid enlargement of the growth, and its softening and necrosis. When hemolysis continues, the red coloring matter may be replaced by others—brown, yellow, or gray—depending upon the lipid content of the tumor. Transitions from red degeneration to total necrosis are not uncommonly seen. Murray's theory, however, has not obtained general acceptance. Especially

does Ahlstrom deny that the lipoids are increased in this condition, since in 3 cases he found that they were either decreased below normal or absent. The other theories that have been advanced to explain this picture are based upon the diminished nutrition which results from thrombosis, or venous stasis and consequent hemorrhage.

FATTY DEGENERATION.—Fatty degeneration of uterine fibroids has occasionally been described but appears to be a rare condition. It occurs almost invariably in cases which have had large areas of hyaline degeneration which have become liquefied in the center. Local factors apparently are responsible for the fatty changes. Lipoid is present, either in the form of lipid fat or lipid soap. It is a product derived from muscular or connective tissue degenerations; the cytoplasm passing through the various phases of cloudy swelling, granular and hyaline degeneration, and finally to fatty necrosis. The fat globules are deposited in the muscle fibers, and fat is seen in the white blood cells in and outside of the lymphatics. There are signs of vascular degenerations, engorgement, thrombosis, and fibrine deposits in the vessels. Cholestrine crystals may be found in the liquefied cavity in the center.

The presence of fat is not always a sign of degeneration, since it may be deposited in fibroids which, to casual inspection, do not appear unusual. Only on careful scrutiny do you find suggestions of fat. These tumors form a distinct type and are called fibrolipomyomata, or lipomyomata. Knox's case is typical of the series, that is, a large globular tumor of typical adipose appearance, subdivided into a number of small areas by bands of smooth muscle and connective tissue. The tumor sprang from the uterine wall. R. Peterson described a submucous lipomyoma which was accidentally discovered when operating for uterine prolapse. The subject was early reviewed in 1903 by Seydel, who collected only 11 cases.

The gross appearance of fatty fibroids is variable. The whorled appearance may be absent, and the tumor may contain material resembling melted butter; or the whorled structure may be preserved, with a number of small fatty areas, which are sufficient to give a cut surface a pale yellow color. The consistency varies with the degree of degeneration, and the more fat laid down, the softer the tumor. The growth may be tinted by soluble blood pigments. Grayish red flocculi, or streaks of blood, may be seen which result from hemorrhage. This form of degeneration does not present distinctive symptoms.

MALIGNANT DEGENERATION.—The old idea that fibroids did not undergo malignant degeneration has been completely disproved as the result of routine examinations of large series of cases. Careful examination of fibroids has shown that operation is often justifiable merely because of the average percentage of malignant changes. Thus if malignant alterations occur in 3 or 4 per cent of fibroids, the patient will be well insured by an operation which may be done with less than one per cent mortality. The great majority of gynecologists agree

that malignant changes are the most important condition that occur in fibroids.

Sarcomatous degeneration of fibroids is usually considered as the only type of malignant degeneration. It is equally important to bear in mind the frequency with which carcinoma of the body is found in uteri presenting myomatous tissue: indeed, many, as Deaver, consider this the most important and serious degeneration initiated by a fibroid.

Sarcoma.—The frequency with which sarcoma is found varies widely, since it is dependent not only upon the personal equation of the pathologist and his capacity for diagnosing malignant conditions, but also upon the thoroughness with which he studies all sizes and types of fibroids. Sarcomatous areas may easily be overlooked on gross inspection, unless the tumor is carefully and completely sectioned. The need for such a careful routine examination of fibroids is well illustrated by the findings of Winter in his two separate series of cases. In 1907, he found that sarcoma was present in 3.2 per cent of 500 cases in which only grossly suspicious areas were subjected to microscopic study. When every area of tissue showing variations from the normal was studied in the second series of 253 cases, the percentage of sarcoma was raised to 4.3 per cent.

The frequency of sarcomatous changes in fibroids is usually given at a lower figure, undoubtedly because fibroids are not usually subjected to a careful routine microscopic study. It has variously been reported as follows:

SARCOMATOUS CHANGES

Frequency of	Fibroids	Percentage sarcoma
Fehling	409	2
Martin	205	2 (4 cases)
Cullen	1400	1.2 (27 cases)
Noble	337	1.8
Webster	210	1 (2 cases)
Cullingsworth	100 (myomata)	1 (2 cases)
McDowell	1000	2 (20 cases)
Scharlieb	100	1.6 (6 cases)
Haultain	120	1.6 (2 cases)
Hirst	189	1.5 (3 cases)
Deaver	345	1.2 (4 cases)

Collectively, this totals about 2 per cent, but Winter feels, however, that if all tumors were carefully examined, the true frequency of this condition would be about 4 per cent. Others, as Cullen, state that the percentage may be much higher, since formerly only the cases which showed gross anatomical changes were studied microscopically.

The number of reported cases of sarcomatous degeneration is constantly growing. The chief discussion concerns the nature of the

process, whether sarcoma develops secondarily to the fibroid, or whether it really represents a primary process. Indeed, the possibility of sarcomatous alteration of fibroids has been questioned by many. Clinical data has supported microscopic evidence of sarcoma developing in fibroids, by many instances in which the growths recurred after operative removal. Polypi which were thought to be harmless have also been followed by recurrences, which were proved to be of a sarcomatous nature. Martin holds that many cases believed to be primary sarcoma are, in reality, secondary changes in fibroids that were not recognized, and that the true frequency of sarcomatous alterations in fibroids is at least 4 per cent.

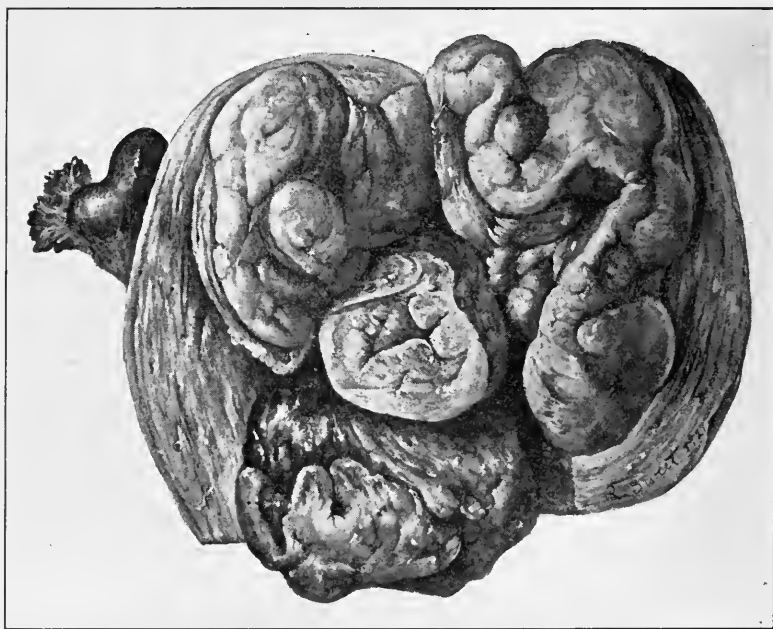


FIG. 31.—MULTIPLE FIBROIDS WITH SARCOMATOUS DEGENERATION IN THE LOWEST TUMOR.

Gross Appearance.—Early sarcomatous alteration cannot be recognized macroscopically. When the malignant state is well established, it is usually easy of recognition (Fig. 31). The coarse, pink, fibrillary arrangement of the fibroid is wholly, or in part, replaced by a uniform, homogenous, yellow or buff-colored tissue. The sarcomatous area is usually sharply demarcated from the surrounding tissue, although occasionally it merges with the surrounding structures. It may present a porous appearance, or may contain large or small cysts. Most frequently it is softened and is rich in tissue juices. If hemorrhage has occurred in the growth, the cut surface is brownish in color, sometimes gradually fading to a yellow brown when blood pigments have been deposited. The sarcomatous alteration commonly begins in the central

portion, rarely in the periphery. It is usually followed by a coagulation process. With the advance of the growth, secondary foci are scattered throughout the uterine wall or in other myomatous nodules, and sarcomatous polypi may project into the uterine cavity. Sarcoma may occur in subperitoneal, submucous or interstitial tumors. Many claim it is more frequent in submucous types. This is substantiated by Winter, who found that 8.7 per cent of 126 submucous fibroids had become sarcomatous, while Holmes gave 5.8 per cent in his series. Cullen's experience, however, is to the contrary, since sarcomata in

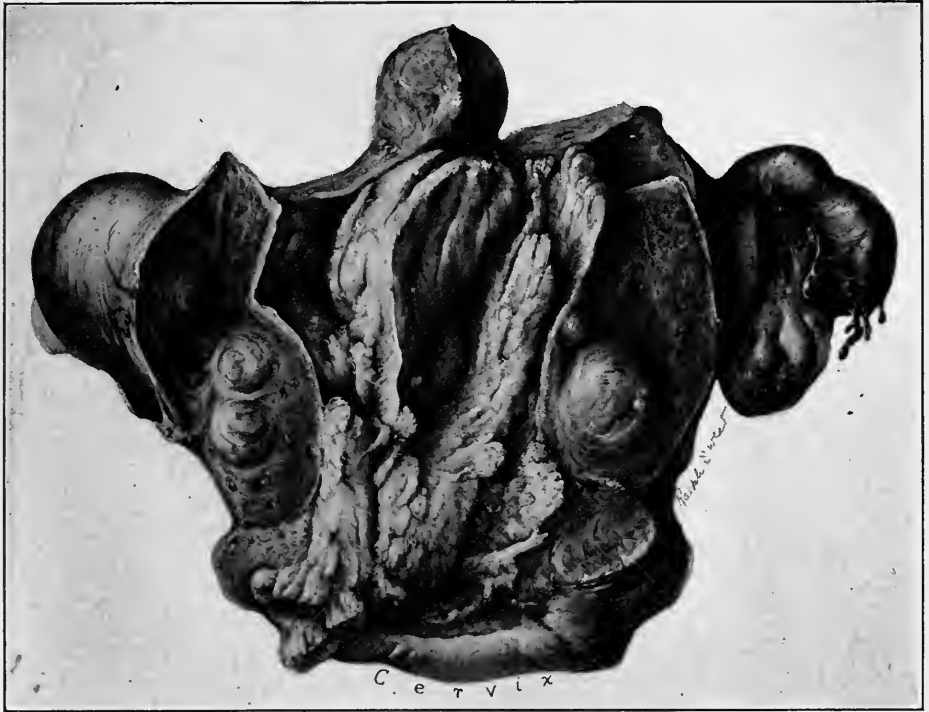


FIG. 32.—MULTIPLE FIBROIDS WITH ADENOCARCINOMA OF FUNDUS.

interstitial and subperitoneal growths were far in excess of those in the submucous tumors.

RELATION OF UTERINE FIBROIDS TO CARCINOMA.—Carcinoma is not a degeneration of a fibroid, as it must arise from epithelium. This association has been frequently observed, and it is worthy of comment that the cancers of the uterine body are much more numerous than those of the cervix in fibroid uteri. While fibroids may be invaded by cancer of the cervix or of the uterine body, there is evidence to believe that the great majority develop as a result of the changes due to the presence of the benign tumor. Many have called attention to a hyperplastic condition of the uterine mucosa which gradually becomes malignant in fibroid cases (Fig. 32). It would seem that this is a fair assumption and one

which is also suggested by the known tendency of chronic nutritional and irritative influences to excite malignant changes. Weibel, in 1913, states that in a series of 1,000 fibroids, carcinoma of the uterine body was found in 20. Noble emphasized the greater relative frequency of cancer of the fundus in fibromatous uteri. He found that cancer was present in 2.8 per cent of 4,880 cases of fibroids collected by him. Cervical cancer occurred in 1.29 per cent, and cancer of the fundus in 1.54 per cent. In 337 cases of his own series, cancer of the cervix occurred in 1.4 per cent and cancer of the corpus in 2.6 per cent.

While there is a difference of opinion concerning the relative frequency of carcinoma of the cervix to that of the body in various series, there is no doubt but that cancer of the cervix is many times more frequent. In our experience, carcinoma of the cervix has been noted twenty times for each carcinoma of the uterine body. Cullen's series gives the highest percentage of cancers of the fundus, occurring once to four cases of cervical cancer. Martin found the proportion in his series as one cancer of the fundus to ten cancers of the cervix. In 2,097 cases collected by Hofmeier, Krukenberg, Freund, and Winter, there were 179 cancers of the uterine body, a relation of 12 cervical carcinoma to 1 cancer of the fundus. On the contrary, all agree that more cancers of the body of the uterus occur in fibroid uteri than do cervical cancers.

This is emphasized by the following statistics: Kerr found only 1 cancer of the cervix in 200 fibroid cases, although there were 6 cancers of the fundus in the same series; Kelly and Cullen found 43 uterine cancers in 1,400 fibromyomatous uteri. Of these, 25 were carcinomata of the uterine body. Deaver found 11 cancers in 345 fibromyomata of the uterus. Of these, 6 were cancers of the body. Winter, in Königsberg, found 23 carcinomata in fibromyomatous uteri, of which 8 were in the corpus. In his Berlin series, he encountered 36 cases of which 23 were in the fundus. Geuer reported 46 carcinomata plus fibroids, of which 33 were in the body. Martin found 9 carcinomata in fibroids of which 7 were in the body. Hofmeier noted 17 cancers in fibromyomatous uteri, of which 9 were corporeal. If the presence of fibroids did not favor the development of adenocarcinoma, we should expect the relation of cervical to corporeal carcinoma to remain unchanged.

Piquand and Winter think that the presence of fibroids increases the frequency of cervical carcinoma. The evidence for this view is less conclusive. Winter found, in compiling his own cases with those of Hofmeier and Freund, that carcinoma of the cervix occurred 25 times, or 2 per cent, in 1,270 fibromyomatous uteri.

THE EFFECT OF UTERINE FIBROIDS ON NEIGHBORING AND DISTANT ORGANS

On Uterus and Adnexa.—The uterus hypertrophies just as in pregnancy under the influence of fibroid growths in its body. The hypertrophy is more marked in the interstitial types than either the submucous or the subperitoneal. It may occasionally present tremendous size. Kelly reports a case in which the uterus weighed 645 grams after the removal of the tumor—an increase of fifteen times the normal weight. The outline of the uterus changes according to the type of tumor contained within it. The form is usually asymmetrical, yet the outline may resemble normal in the case of large interstitial and submucous growths. This may lead to confusion with the diagnosis of pregnancy. The uterine cavity is much lengthened in interstitial and submucous tumors, and may be distorted in both shape and direction.

The individual muscular fibers and the intermuscular cellular tissue are markedly hypertrophied as seen by a microscopic examination. It may not occur, however, in the myometrium which lies between small and numerous interstitial fibroids, probably because of the pressure exerted by the tumors. The outer coatings of the uterus present cells which are tremendously enlarged and which may readily be confused with those of midterm pregnancy. Individual muscle cells have attained a length of 166μ , and a breadth of $13\frac{1}{2}\mu$.

The position of the uterus will depend upon the size and situation of the growths. Displacements may occur in any direction. Small fibroids scattered throughout the organ may not change the uterine position. A tumor on the posterior wall will tend to push the uterus against the symphysis. A fibroid on the anterior wall may cause a uterine posterior displacement, and the fundus may be forced down into the posterior cul-de-sac. A fibroid developing on the lateral surface or between the folds of the broad ligament usually forces the uterus to the opposite side. The weight of a large, submucous, pedunculated fibroid may cause descent of the uterus, and even inversion may follow as a result of nature's effort to expel the growth. A cervical fibroid will carry the uterus with it high into the abdominal cavity. The uterus may become twisted on its long axis and present high degrees of torsion; rarely the uterine body may be partly or entirely separated from the cervix as a result of this complication.

The changes in the uterine mucosa vary, since it may be affected in the same manner as the muscularis, both by hyperemia and altered ovarian function. Tumors lying in the uterine cavity may thin out the overlying mucosa by mechanical pressure until little or none of it remains over the prominent parts of the growth. In such cases, the mucosa surrounding the growths is much thickened. Tumors which

are denuded of surface epithelium are more likely to undergo degenerative changes, since this condition favors the development of infectious processes.

The mucosa may be unaltered in appearance if the tumor does not encroach upon it, or it may appear bright red from capillary injection or from foci of ecchymosis. The hemorrhagic areas turn brown or black in color as they become older.

Dilatation of the veins of the mucosa is frequently found, but definite bleeding vessels are rarely seen. The general picture suggests a marked congestion, which is confirmed by the gradual oozing which is seen from the vascular system. Edema of the mucosa is often very marked, and serous fluid escapes from the cut surfaces. It is confined to the mucosa and usually limited to small areas. This may occur with any type of tumor. The glands may be normal in size. Occasionally they run parallel to the surface instead of at right angles, especially over the less prominent portion of submucous tumors. The glands are usually dilated. Sometimes they project as small cysts into the uterine cavity. They are often arranged in rows, and contain a clear, limpid fluid in which are small, yellow bodies composed of exfoliated epithelial cells. The surface epithelium may be absent over markedly dilated glands. Glandular hypertrophy may be found when a submucous tumor is present. It rarely occurs with the subperitoneal form. Even though the uterus is elongated, the mucosa rarely hypertrophies in this class of tumors; more frequently the mucosa is atrophied. The most striking changes in the uterine mucosa are seen with the submucous tumors. Atrophy of the endometrium may follow counter pressure of such a growth on the opposite side. This may lead to stenosis of the cavity and may be followed by hydrometra, pyometra, or hematometra. Landau has described a case in which serial transverse sections of the whole uterus failed to show microscopic evidence of a uterine cavity.

Mucous polyps are commonly found in association with fibroids. They may occur at any part of the wall, but usually present as a single growth attached to the fundus. The polyp is often a heaping up of the mucosa. As it enlarges, it becomes pedunculated. It consists of a core of whitish yellow, semitranslucent tissue, and contains small dilated glands which shine through the uterine mucosa, resembling minute cysts. The tip of the polyp is usually dark red in color, and shows small hemorrhagic areas.

Endometritis is rarely noted, even in the presence of definite inflammation of the appendages. Exceptions occur when there are sloughing mucous fibroids or when an involuting puerperal uterus is invaded by secondary infection. Tuberculosis of the endometrium has been found without invasion of the fibroid. Kelly and Cullen noted it in 7 out of 1,428 cases.

On Tubes and Ovaries.—Inflammatory conditions are frequently seen and often arise from pressure. Tait found appendage disease in 54 per cent of cases; Fabricius states that both tubes are likely to be affected in the presence of the larger tumors. Cullen found adhesions binding both tubes in 423 cases out of 934. The adhesions were often sufficiently dense to cause occlusion. Friction between the tumor and the pelvic peritoneum abrades the delicate epithelial cells with the resultant formation of slight adhesions. Blocking of the drainage of the uterine cavity or tubes will cause back pressure, and the secretions dam back and result in inflammatory changes. McDonald's series of 280 cases presented 137 with inflammation of the adnexa. Webster

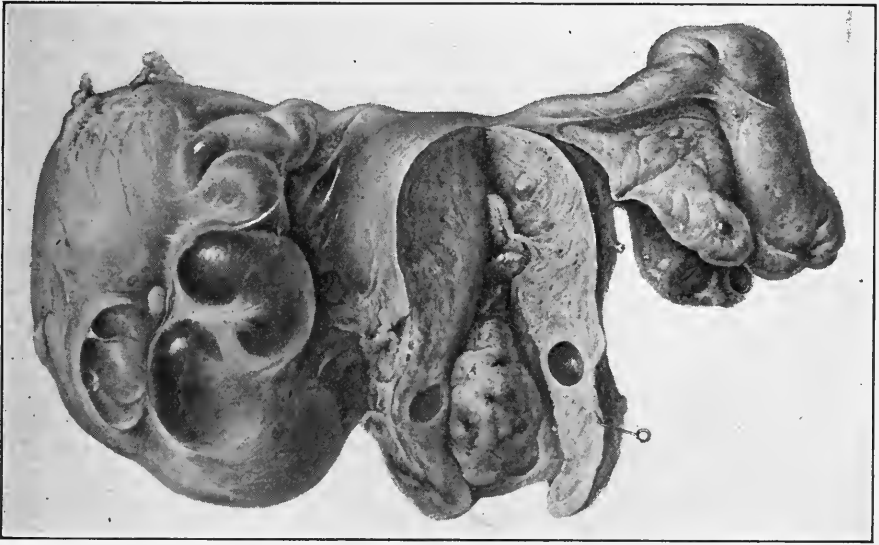


FIG. 33.—ADNEXAL COMPLICATIONS WITH FIBROIDS.

found tubal disease in 99 of 210 cases. Meredith reports tubal disease in 56 per cent and chronic ovaritis in 46 per cent of Lawson Tait's series. Sloughing fibroids and infections introduced through the cervix are often responsible for the production of pelvic adhesions (Fig. 33). Cullen noted hydrosalpinx 88 times, hematosalpinx 100 times, and pyosalpinx 41 times in a series of 934 cases (24 per cent of tubal disease). Tubo-ovarian cysts occurred 5 times, and tuberculous salpingitis 14 times in the same series of cases. When there is no definite inflammatory change, the tubes may present as normal, or may be stretched out over the tumor and be enormously elongated.

The ovaries were adherent and showed some pathological alterations in 438 of 934 of Cullen's series. Old pelvic adhesions were found in 48.6 per cent of 148 autopsies of women presenting fibroids, at the Johns Hopkins Hospital. Pelvic and abdominal adhesions presented in 7.6 per cent, giving a total of 56.2 per cent of cases, coming to

autopsy in which fibroids were associated with adhesions of some character. There were 184 ovarian cyst formations in Cullen's series. These cases presented the following conditions:

RETENTION CYSTS	
Small ovarian cysts.....	44
Graafian follicle cysts.....	68
Corpus luteum.....	34
PROLIFERATION CYSTS	
Multilocular cystadenoma.....	9
Papilocystadenoma	12
Adenocarcinoma.....	8
Dermoids	17
Parovarian cyst.....	19
Fibroma.....	3
Enlarged ovaries.....	2
Ovarian abscess.....	6

On the Pelvic Organs.—As the tumor grows, it is likely to exert pressure on the structures which normally lie in the pelvis. Pressure symptoms, as a rule, develop slowly. They are most common in the case of large tumors which have remained within the pelvis, although serious complications often arise from pressure by intraligamentary tumors, often of small size. Pedunculated subserous growths may cause pressure symptoms when they have become incarcerated in the pelvic cavity. The bladder, ureters, and rectum are most likely to be affected.

The bladder symptoms vary. Often the structure is prevented from filling in a normal manner. A fibroid of the anterior uterine wall may compress or elevate it. Occasionally it is lifted out of the pelvis and when distended may reach as high as the umbilicus, a point to be kept in mind when making an incision directly upon the growth. Adhesions between the fibroids and the vesical peritoneum are frequently found. Encysted peritonitis containing pockets of clear serous fluid is not infrequently noted. The bladder sometimes becomes sacculated as the result of pressure. The mucosa of the displaced bladder is normal unless there has been obstruction to the urethra, when retention of urine and cystitis are not uncommon. The bladder wall is often thickened in such cases as the result of effort to overcome the partial blocking of its drainage. The vesical symptoms in association with displacement from the fibroid vary from increased frequency of micturition with only partial emptying of the viscus, to difficulty in voiding and even to complete blockage. Bladder symptoms may be the first complaint made by the patient who has a uterine fibroid. Occasionally they are the only subjective symptoms.

The vagina may also be displaced. Sometimes it is drawn up and greatly elongated; in other cases, it may be pushed down by the weight of a tumor not completely fixed in the pelvis; and very rarely it may be almost inverted.

The ureters are frequently involved. Their lower insertions may be displaced by growths which encroach upon the base of the bladder. Intraligamentous tumors may displace them downward, outward, or upward. Sometimes the ureter will be found upon the top of an intraligamentous or cervical fibroid in a position quite remote from the normal one. Pressure on the kidney may cause hydro-ureter, hydro-nephrosis or even destruction of the kidney, and the literature indicates that these complications are more common than has hitherto been emphasized. Cullen found hydro-ureters in 11 cases of his series. Welch, in 148 autopsies on fibroid cases, found obstruction 5 times. Knox has shown that some obstruction was present in a large proportion of his series of cases. As a rule, the ureters are disturbed only when the growth is retroperitoneal or spreads out between the folds of the broad ligament.

The rectum may be compressed, although complete obstruction probably never occurs unless there are secondary complications. Auto-intoxication and anemia have been ascribed to partial obstruction by impacted fibroids, and chronic constipation and difficult defecation are quite common. Hemorrhoids are frequently seen in fibroid cases. Adhesions to the rectum and sigmoid colon are often found. This complication occurs most commonly when there is pelvic inflammatory disease, yet is often seen when the appendages are normal. The fixation may be so dense that the nourishment of the tumor is supplied by the mesenteric vessels of the bowel. If the growth burrows beneath the mesosigmoid, the rectum and sigmoid may be elevated into the abdominal cavity. Lateral displacement is common in cases in which there is a left-sided, broad ligament growth. Prolapse of the rectum or downward displacement of the canal is relatively infrequent. Pelvic abscesses sometimes occur in fibroid cases, with the abscess draining directly into the bowel. We have seen several cases where a carcinoma of the sigmoid or rectum coexisted with a fibroid of the uterus.

Effect on Distant Organs—CARDIOVASCULAR CHANGES.—For many years, it has been well known that the mortality following the removal of fibroids has been greater than should be expected merely from the removal of the tumor. Even at the present time, in spite of the remarkable development of operative table technic, thrombosis and embolism often lead to death. Kazprezik, in 1881, called attention to the cardiac weakness found with fibroids, and Hofmeier, in 1885, emphasized its occurrence especially in the larger tumors. Many pathologic findings have been described by the pathologists and the clinicians. Brown atrophy and fatty degeneration of the heart, atheroma of the blood

vessels, myocarditis, and endocarditis are commonly observed. The clinician often finds cardiac murmurs for the most part of hemic origin. Roger Williams reports the following findings in the heart of 32 autopsies of women with fibromyomatous uteri: valvular heart disease, mostly chronic, 6 cases; fatty degeneration, 5 cases; hypertrophy and dilatation, 3 cases; atheroma of the aorta, 3 cases; small heart, 3 cases; normal heart, 12 cases. The following table shows the frequency of cardiac lesions:

Authority	Number cases	Per Cent
Strassman and Lehman (Gusserow) ..	71	48.8 showed cardiac pathology
Fleck.....	325	48 " " "
Boldt.....	79	47 circulatory disturbances
Wilson.....	72	46 " "
Webster.....	210	25 " "

Pallanda, as a result of his study, concluded, in 1905, that in the natural evolution of fibroids, pulmonary embolism, thrombosis of the pelvic veins, cardiac lesions, and sudden syncope followed in 11 per cent of cases. Wilson believes that myocardial degeneration was responsible for death in 4 of the fatal cases of his series. Of Boldt's series, 3 of the 5 cases that died after operation succumbed from cardiovascular degenerations. Fenwick, in 1888, reported 22 cases of large cystic abdominal tumors in which fatty degeneration of the heart was found at autopsy. Fleck, from his 325 cases, concluded that brown atrophy of the heart muscle is characteristic of fibroids without hemorrhage and that fatty degeneration of the myocardium is found with hemorrhage. In all of his autopsy material, definite changes were found and cardiac pathology was proved in 36 per cent of 133 cases which had not had hemorrhage. Cardiac changes were demonstrated clinically in 34.6 per cent of cases in which there had been no hemorrhage. They were found in some cases in which the tumor was of small size. From these statistics he concludes that some other condition besides loss of blood was responsible for the condition of the heart.

Yet all do not agree as to the frequency of cardiac complications. Winter reports the clinical results in a series of 266 fibromyoma cases in which the cardiac findings were made by an internalist. The heart was normal clinically in 60 per cent of cases, while 30 per cent presented murmurs which were thought to be of hemic origin. Cardiac dilatation and hypertrophy were found in 6 per cent of cases, and most of these were thought to be due to anemia. True valvular disease was diagnosed in only 1 per cent of the series.

There is much controversy as to the cause of these lesions. Are these primary changes in the heart and blood vessels due to the same cause which produces the tumor, or are they merely secondary results

and symptoms of the tumor? Formerly, nearly all believed in the so-called "fibroid heart," because of the frequent association of heart changes and the large number of deaths both before and after operation which resulted from cardiovascular lesions. Recently, the belief has developed that many of the changes are secondary to the anemia which results from hemorrhage or from disturbance of digestion induced by pressure of the tumor. McGlinn, in 1914, presented a statistical study which denied the existence of a specific "fibroid heart." He based his work on the records of 5,700 autopsies. For each case with a uterine fibroid, he took as control another case of the same age and race, without a fibroid. There were 131 fibroid cases which constituted 20.75 per cent of the 632 female bodies. He studied his cases as a unit and subdivided according to the decade of their age and concluded that a definite entity of a "fibroid heart" could not be sustained from his findings. While the matter cannot be regarded as finally settled, there is little evidence in favor of the "fibroid heart." All are agreed, however, that the proportion of deaths from thrombosis and embolism in fibroid cases is more frequent than in any other gynecologic condition, with the possible exception of the fibrosis uteri cases.

KIDNEY CHANGES.—Mention has already been made of the pressure effect of fibroids upon the ureters. If the block causes back pressure along the ureters into the kidney, a hydronephrosis or pyonephrosis may result. This mechanical interference is fairly common, and may be of considerable clinical importance. Knox has reviewed a series in Kelly's service. Of great interest, however, are the urinary disturbances when mechanical interference is not a consideration, as may be seen when the fibroid is small or located far from the ureter. The theory has been advanced that toxic effects from the fibroid act upon the kidney parenchyma and accounts for albumin, casts, and pus cells which show in the urinary analysis. This form of kidney irritation may occur in women of normal blood pressure, and who do not present cardiac pathology. The toxic theory is rather borne out by the fact that the symptoms disappeared only after the fibroid was removed, even though it did not exert pressure upon the ureter. When the kidney damage has been long continued and fairly extensive, the urinary symptoms may persist for some time even after the removal of the tumor. Webster found renal disease in 30 per cent of his cases and held that the factors which produced these changes are identical with those causing cardiovascular disturbances.

NERVOUS SYMPTOMS.—This group of symptoms is often overlooked, yet is very apparent in individuals who appear susceptible to even slight absorption of toxic products. Numerous observations tend to the belief that such patients are also liable to the toxicosis of pregnancy. The nervous symptoms may be mild, or so severe that they result in mental impairment. Temporary insanity has occurred in

women with fibroids and has cleared up after hysterectomy or myomectomy. The frequent association of these symptoms even in women of stable nervous system is too frequent not to be considered as a causal effect. The thyroid is also affected by a growing fibroid and is marked by tachycardia, sweating, and the presence of a goiter. The stormy convalescence with the rapid pulse and diarrhea may well be due to disturbance of the thyroid balance after the operative removal of a fibroid.

SYMPTOMS

Fibroids may be of considerable size and cause no symptoms whatsoever, and the presence of the tumor may be discovered by accident. Symptoms arising from the growth may present a wide range of variation. They may come primarily from the uterus, or may result secondarily from effects upon adjacent or remote structures. The primary symptoms may be grouped under the headings of hemorrhage, leukorrhea, pressure, pain, dysmenorrhea, sterility, disturbances in pregnancy, labor, or the puerperium. The secondary symptoms include anemia, nervous disturbances, thyroid, kidney and cardiac symptoms, and complications resulting from degenerative changes, disturbances in circulation and mechanical injury to the tumor.

Hemorrhage.—Hemorrhage is probably the most common symptoms of fibroids. It does not occur, however, in all cases, even in those which present growths of considerable size. Hemorrhage usually occurs as menorrhagia, since intermenstrual bleeding is comparatively rare. The menstrual flow may be prolonged or excessive in amount, or both conditions may exist together. Occasionally, the interval between the periods is so shortened that there are but few days when the patient is entirely free from bleeding. The menorrhagia depends upon a number of factors, chief of which is the circulatory disturbance and the congestion of the uterus incidental to the growth of the tumor (see blood supply of fibroids, p. 80). It is generally favored by the presence of hyperplasia of the endometrium and is precipitated often by nature's effort to expel a submucous tumor. It would appear that there are certain mechanics of the hemorrhage in fibroids. When the tumor is purely interstitial, the hemorrhage usually increases *pari passu* with the size of the tumor. If it grows toward the peritoneum the bleeding may lessen and even disappear when the tumor is extruded as a pedunculated subserous fibroid. On the contrary, the bleeding increases disproportionately as the interstitial form approaches the uterine cavity. When the growth becomes frankly a submucous tumor, the bleeding may be most severe. Intermenstrual bleeding occurs when the submucous fibroid appears at the cervix.

Practically, however, the mechanics holds true chiefly in theory, since fibroids are usually multiple and all three varieties may be found in the same uterus. Especial emphasis should be laid upon the fact that submucous growths occasion hemorrhage out of all proportion to the size of the tumor. A single submucous fibroid the size of a pea may occasion more alarming bleeding than very large interstitial or subperitoneal tumors. Hemorrhage is often so profuse and of such long standing as to occasion severe anemia, since there is not time for recuperation in the few days in which there is no bleeding. The hemoglobin may fall below 20 per cent and the red blood count to less than 2,000,000. Ordinarily, the hemoglobin is between 40 and 50 in cases which come for treatment presenting this symptom. The patient is pale, with waxy, transparent skin, and suffers from breathlessness. Edema of the face, most marked about the eyelids, is associated with the anemia. Secondary symptoms readily follow. Excessive bleeding may indicate the development of malignant or degenerative changes, although it rarely appears as the sudden flooding noted in carcinoma. It uniformly occurs when submucous growths become infected.

A noteworthy feature of fibroids is that they cause a postponement of the menopause. Patients menstruating regularly past the age of fifty usually have fibroids. It is believed that 95 per cent of patients menstruating regularly and without interruption at fifty-four have fibroids. The history of bleeding in fibroids differs greatly from that in carcinoma. The hemorrhage from carcinoma often comes years after the menopause. The postponement of the menopause, therefore, strongly suggests the presence of fibroids. This delay in the climacteric is common to all varieties of fibroids and is not confined to the submucous growths.

Internal hemorrhage may occur from the surface of subperitoneal fibroids. It comes from rupture of one of the thin-walled veins which spread over the peritoneal surface of the tumor. Steinbüchel records a case of intraperitoneal hemorrhage and collapse following torsion of a pedunculated tumor with a history that was most suggestive of a ruptured ectopic pregnancy. Stein reports a fatal case from intraperitoneal hemorrhage from the bursting of a vein in the subserous tumor.

Leukorrhea.—Leukorrhea is a symptom of little diagnostic value. It usually represents the transudate from distended capillaries of submucous growths or a glandular secretion from a hyperplastic endometrium. It may, however, occur from old cervical infection. It may be thin, watery, and occasionally bloodstained, in the presence of cystic tumors. Often it is extremely irritating and occasions acute pruritus. The discharge is foul smelling when there is ulceration or gangrene of the tumor. Like leukorrhea in general, it is most noticeable just before and after menstruation.

Pain.—Pain is not a necessary symptom of fibroids, although it usually occurs from one cause or another. It indicates, as a rule, the advent of some degeneration or an infection. Cullingsworth found it in two-thirds of his necrobiotic cases, in three-fifths of cystic fibroids, and in one-third of edematous tumors. Pain is extremely common in growths presenting malignant changes. It also results from associated pelvic inflammation, or from pressure of the growth upon normally tender areas. The pain is also worse at the menstrual period. Inter-menstrual pain may come from the uterine contractions which attempt to expel a growth from its body, as when an interstitial tumor is about to become either subserous or submucous and when submucous tumors have been so detached that they represent a foreign body. The frequency with which pain occurs with malignant changes should be considered as of diagnostic value and should at least arouse the suspicion that the growth is no longer benign.

Dysmenorrhea.—As we have noted, pain may occur from uterine contractions in the effort to expel a submucous growth or blood clots which result from excessive bleeding. This type of dysmenorrhea is coincident with the flow and is frequently described as resembling the pains of labor. Dysmenorrhea is not common with interstitial or subserous tumors and when present may be difficult to explain unless there is associated pelvic peritonitis. It is normally present in adenomyoma (q. v.).

Pressure Symptoms.—Pressure symptoms are not uncommon and are dependent upon the size and position of the tumor. A small intraligamentous tumor may occasion far more symptoms when incarcerated than a large pedunculated subperitoneal growth that is free in the abdomen. Nerve pains in the lower limbs may be the only complaint. This is well illustrated by a recent instance in our service in which the woman complained only of numbness and tingling in her left leg for six months. There were no menstrual disturbances and the patient was totally unaware of a large tumor. At operation, multiple interstitial and subperitoneal fibroids were found and, jammed in the cul-de-sac, was a partially impacted tumor, the size of an orange, which was occasioning the pain.

Bladder Symptoms.—These have already been mentioned. In spite of its close relation with the uterus, disturbance of its functional activity is rather infrequent, on account of its mobility and ability to distend in the plane of least resistance. Fibroids confined to the pelvis are more likely to occasion pressure symptoms. The pressure is diminished and the symptoms tend to disappear when the growth has so enlarged that it rises into the abdominal cavity. As long as the distensibility of the bladder is not interfered with, and there is no encroachment which limits the extent of its capacity, the organ is very tolerant of displacement. The bladder may be found adherent to the anterior surface of large uterine tumors, and may be drawn up into

the abdomen as high as the umbilicus without occasioning any vesical symptoms.

Frequent urination occurs in about 88 per cent of women with fibroids. Only occasionally is tenesmus or dysuria present. There is usually a feeling of weight and discomfort. Retention of urine is not frequent. It occasionally results suddenly because of the impaction of a fibroid uterus. The urethra is rarely compressed, although the lumen may be narrowed from elongation and stretching of the duct.

DIAGNOSIS

The diagnosis of uterine fibroids usually occasions little difficulty. Occasionally, however, it is extremely difficult, especially in the small submucous and large interstitial types of tumors. The diagnosis is based chiefly upon the results of bimanual palpation, although sometimes it may be made purely by abdominal palpation. The history of the case is most useful in aiding the differential diagnosis, although the pelvic condition finally rests upon the pelvic examination. Symptoms are subjective and objective. Subjectively a woman usually of middle life gives a history of hemorrhage, dysmenorrhea, and other pelvic symptoms which may have extended over a considerable time. The patient may or may not have had symptoms of pressure or be conscious of the presence of the tumor. Often there is a history of sterility or of frequent abortion. The patient usually has gained weight. Emaciation is rarely noted, and is confined practically to the cases presenting enormous tumors. Objectively, there are symptoms of anemia when there has been bleeding of long duration. The skin is pale, yellow and white in the anemia following fibroids in which it differs from the yellow brown of the cachexia of cancer. On bimanual examination, the uterus is enlarged and often of irregular outline. Since fibroids are usually multiple, there are knobs or bosses of subperitoneal tumors. The uterus is usually firm, yet is not always hard nor of irregular outline. Frequently, it is soft and rounded, and may readily be confused with pregnancy and cause much difficulty in the diagnosis. Occasionally the diagnosis cannot be made until the cervix is dilated and a polypoid growth felt within the uterine cavity.

The appearance of fibroids varies so considerably that the question of diagnosis is best presented according as the tumors are large or small.

Diagnosis of Small Fibroids.—Small, submucous, pedunculated fibroids above the level of the internal os are often recognized only after the uterine canal has been dilated sufficiently to admit a sound, or occasionally a palpating finger. The whole uterus is usually more or less symmetrically enlarged and is harder than a pregnant uterus,

although softer than the normal. The enlargement may readily be mistaken for a metritic uterus or that seen in premenopausal congestion. Hegar's sign of pregnancy is absent, nor are there intermittent uterine contractions.

Tumors which present through the cervix may be mistaken for pedunculated sarcoma, or the placental remains of an abortion. Their appearance varies according as the tumor is covered, or not covered, with mucosa. Tumors which are sensitive to pain are covered with a deeply injected mucosa. An inverted uterus is readily recognizable in the majority of cases. The peduncle usually is palpable as a stalk coming down through the cervical canal. Ulcerated or gangrenous tumors may readily be confused with malignant growths. In case of doubt, the patient should be examined under anesthesia and the cavity of the uterus explored with the finger or the sound unless there are contraindications for anesthetics. It is very difficult to diagnose small, submucous, nonpedunculated tumors. Even after the cervix has been dilated, they may not be recognized with a curette or sound, although this is unusual. The uterus is increased in size and more rounded than normal. There is history of bleeding.

Small interstitial tumors may escape recognition, although they usually cause asymmetry of the uterus. When low down, they may bulge into the cervix and rarely simulate inversion.

Small peritoneal tumors usually produce a slight bulging on the surface of the uterus. They are more or less movable, but their form and consistency depends on various conditions. Pedunculated growths may simulate ovarian swellings, when the tumor is pedunculated and projects from one side of the uterus. The diagnosis is easy when both ovaries can be palpated, yet this may be impossible.

Intraligamentous growths are readily diagnosed. They are usually situated low down in the pelvis and come within easy reach of the examining finger. Sometimes they even project into the vagina.

Diagnosis of Large Uterine Fibroids.—The diagnosis usually offers no difficulty when the tumor is irregular in outline. When the growth is subperitoneal, its connection with the uterus can usually be demonstrated by an assistant making traction on the pedunculated growth while the surgeon makes a bimanual examination of the uterus. This type of tumor is frequently confused with ovarian cyst. Cysts of large size with long pedicles usually go to the center of the abdomen. Uterine fibroids which are regular in outline may give the greatest difficulty in differentiation from pregnancy.

The examination should proceed according to the accepted methods of inspection, palpation, percussion and auscultation.

INSPECTION.—This frequently gives diagnostic aid. A fibroid large enough to distend the whole abdomen is commonly located more or less on one side of the median line, yet this is not invariable. If small nodules are

seen through the abdomen, there is strong presumptive evidence of fibroid tumor. The contour of the abdomen usually drops suddenly to its normal level above the upper confines of the tumor, while, in ovarian cysts and pregnancy, the descent is more gradual. A linea negra may be present, although rarely as well marked as in pregnancy.

PALPATION.—The outline may be regular or irregular. Irregular shapes rarely give trouble in diagnosis. Fibroids are essentially uterine growths. On pushing the tumor from side to side, the uterus should be felt to move coincidently. Pedunculated nodules on a tumor mass are strongly presumptive of fibroids. The diagnosis is more confusing if the growth is detached from the uterus and has become parasitic. Intermittent contractions are usually absent; probably they occur only in soft fibroids. Colostrum is sometimes seen in the breasts of women who have never had children. Therefore, its presence may not differentiate absolutely between fibroids and pregnancy.

PERCUSSION.—The percussion note is flat unless the growth is covered with distended intestines. The flanks are resonant unless the abdomen contains free fluid. Movable dullness is apparent in ascites and in subperitoneal tumors which are large and mobile.

AUSCULTATION.—This is chiefly of value in excluding the presence of a fetal heart in large symmetrical uterine tumors. A uterine souffle is usually heard at the sides, although it may be present over the surface of the tumor. It is not of diagnostic value, since it occurs in all conditions which have enlarged veins of the broad ligament.

VAGINAL EXAMINATION.—The vaginal mucosa seldom gives a color which may be confused with the changes seen in pregnancy. Occasionally it presents a bluish color, yet only most rarely does it have a purplish tinge. The cases of pregnancy which are most likely to be confused with fibroids do not have the characteristic purple discoloration. The cervix may be variously displaced and is usually of firm consistency. Occasionally its tip is softened. The lower uterine segment is rarely as symmetrical as in pregnancy. At times, however, the outline is perfectly regular and symmetrical. On the bimanual examination, we find an enlarged uterus and, when there are pedunculated subserous growths, masses which appear quite distinct from the tumor. Ordinarily, however, we feel a large uterine mass which is continuous with the cervix.

Differential Diagnosis.—The differential diagnosis lies chiefly between fibroids, ovarian cysts and normal pregnancy. Ovarian cysts are usually softer and more symmetrical than fibroids, although the differentiation is sometimes quite impossible. If two ovaries are felt and there is still a mass in the pelvis, presumably the growth is a fibroid. Pedunculated fibroids, however, may, when of small size, be confused with ovaries.

Uterine pregnancy advanced as far as the fifth month may offer the greatest difficulty in the differential diagnosis. Cases are frequently

operated as tumors and the true diagnosis obtained only when the abdomen is opened. The diagnosis may rest upon hearing the fetal heart, or upon the findings of the X-ray, when the tumor is as symmetrical as the pregnant uterus. Occasionally, even when the abdomen is opened, one may be most uncertain as to the nature of the growth, especially when it has to be differentiated from a two- or three-months pregnancy (Figs. 34, 35). Even with growths of larger size, the surgeon may be convinced that he is feeling the

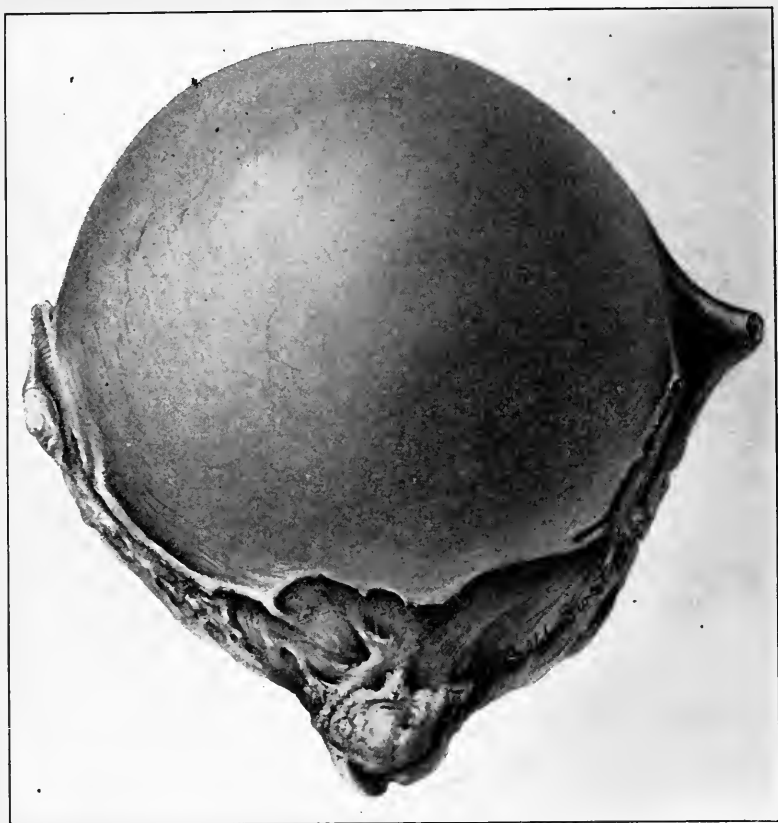


FIG. 34.—CYSTIC FIBROID SUGGESTING FOUR MONTHS' PREGNANCY.

outlines of a fetus. There is no surgeon of experience who has not had cases which proved to be most confusing. Ordinarily, the history of menstruation will help to determine the diagnosis. Yet when there is reason for deception, subjective symptoms are not of value.

Ectopic gestation may be readily confused with fibroids, especially if the pregnancy is situated in an undeveloped uterine horn. It is often quite impossible to arrive at a diagnosis in case there is pregnancy in a double uterus which also contains fibroids. We have seen such a case in which the small tumor in the uterine horn was confused with an ectopic. Both ovaries were present, the uterus was enlarged, the patient had had bleeding, sug-

gesting the extrusion of a uterine membrane. Theoretically, time is necessary to establish a diagnosis of pregnancy. Yet naturally there should be no delay in determining the presence of an extra-uterine pregnancy. While, as a rule, the hardness of the tumor and the absence of the signs and symp-



FIG. 35.—LATERAL VIEW OF FIG. 34. Note cystic spaces in lower pole of tumor.

toms of pregnancy may strongly suggest the nature of the condition, the true diagnosis may not be possible until the abdomen has been opened. When the uterus is greatly enlarged by the tumor, the condition may resemble that of advanced tubal pregnancy, in which there has been death of the fetus and absorption of the liquor amni. The literature contains

many reports of such cases. If doubt still exists after the careful physical examination, X-ray pictures are indicated.

Pelvic inflammatory masses do not usually simulate a fibroid tumor. Occasionally, however, the differential diagnosis is nearly impossible, especially when there has been suppurative peritonitis with extensive exudate which has undergone organization. In most cases, the history aids the diagnosis, yet sometimes it may give no help. In this connection, we should remember the frequent association of pelvic inflammatory and fibroid.

Cancer of the ovary and involvement of the pelvic tissues in general may be differentiated from fibroid by the firmness of the infiltration, its fixity and the lack of outline which is characteristic of fibroid tumors. Occasionally the nature of the condition will not be recognized until the abdomen is opened.

Cancer of the rectum with impaction of feces is often mistaken for fibroids, when the inspissated feces project into the abdominal wall and suggest fibroid nodules. At times, the two conditions exist together.

Sarcoma associated with fibroids may also be confusing. If the disease has extended to the endometrium, it may be recognized by tissue removed by the curette in case the surgeon cures fibroid growths before operation. Often, however, the malignant areas have not extended into the endometrium, or cannot be reached by the curette, and a diagnosis is not made until the tumor is removed and opened, and sometimes not until the advent of metastases which give symptoms.

Other conditions may be mistaken for fibroids. Displaced kidneys or spleen may prolapse to the pelvis and give difficulty in diagnosis. In the presence of adhesions, a diagnosis may not be possible. The notch on the spleen is usually palpable in enlargement of that organ.

Prognosis, without Treatment.—The prognosis of fibroids without removal, X-ray or radium treatment is still a matter of contention. There is no doubt that small growths which are not giving symptoms may cause little or no danger and may shrink during the menopause. Roger Williams, in 1901, concluded that only 1 of 3,000 cases of fibroids proved fatal without operation. This report was based upon the Registrar General's statistics for Great Britain, in which there were 339 deaths attributed to uterine fibroids without operation in a population of 17,000,000 women. In preparing his tables, he calculated that 20 per cent of women over thirty-five years in this series had fibroids. There are many objections to these tables, interesting though they are. Statistics derived from such sources are usually incomplete; especially in fibroids, which do not usually kill *per se* but cause alteration as a result of anemia and kill only rarely because of malignant changes. There is a considerable literature which has reviewed deaths without operation. Pallanda studied 171 such fatal cases. Winter concluded that death resulted from the effect of the tumor after a longer or shorter period in 10 per cent of cases. Noble calculated that 12 per cent of his 2,274

collected cases would have died from degenerations or complications which existed in the tumor if the growth had not been removed. He states that 11 per cent would have died as a result of complications which were present in the uterine appendages or abdomen without treatment. In addition, there existed in his series numerous other complications which caused invalidism. He states, finally basing his conclusions on pathology seen in the operating room, that approximately 30 per cent of all women having fibroid tumors of large size would die in the natural development of the disease or its complications, without surgical interference.

While it may be true that Noble has exaggerated the influence of these tumors, there is abundant evidence that they may not be taken lightly. The long list of fatalities recorded in the literature shows that such women may die without operation. The anemia so often seen in fibroid cases is so marked and so resistant to treatment that in itself it constitutes a considerable source of danger. Degenerative changes in the cardiovascular system and in the kidney are frequent. There is abundant proof that malignant changes in the tumor occasion a mortality at least twice that of surgical interference in proper hands. Complications which occur in the event of pregnancy may kill during labor or the puerperium. Although we are not of the mind to accept Noble's statistics as a whole, we believe that there is no doubt that the danger from leaving tumors the size of a man's fist or greater which are causing symptoms, and the small, but troublesome, submucous growths, is three or four times that which occurs from their removal.

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CHAPTER VI

FIBROIDS

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TREATMENT OF FIBROIDS

The treatment of fibroids has undergone profound revision during the last few years. The great majority of measures formerly advocated as palliative have been superseded by the treatment with radium or the X-ray. The excellent results now obtained by surgical removal make radical treatment the method of choice in the absence of contra-indication to operation. The tremendous reduction in the mortality following operation has been obtained by radical improvements in operative technic and by bringing patients to operation in better condition to stand surgical procedure. Improved methods for the transfusion of blood have done much to make good results possible.

Expectant Treatment.—It does not follow that all growths require active treatment. Many are small and do not present symptoms, and are discovered only accidentally in the course of physical examination. This type of patient should be kept under observation and watched carefully, especially if she is nearing the usual menopause age. The very great majority of small growths shrink markedly in size after the menopause. The patient should be observed at intervals of five or six months and the findings should be carefully reported. Thus the physician will be able to recognize any sudden increase in size of the fibroids and early learn of the advent of symptoms. Both the patient

and the physician should be reconciled to the fact that the menopause is very likely to be greatly delayed.

Systemic Medication.—Medicines usually do little to control the symptoms of fibroid. In the early days of surgery, they enjoyed wide vogue for the control of hemorrhage, yet the results were most uncertain and at best were transient. At the present time, they are useful only as temporary measures and naturally come into competition with the transfusion of blood as a means of getting the patient in better condition for radical measures. Ergot and *hydrastis canadensis* were the drugs usually employed. Ergot was advocated by Hildebrandt in 1872 with the idea that it controlled menorrhagia, reduced the nutrition of the tumor by cutting down the blood supply, and favored the expulsion of submucous, pedunculated growths. Time has shown that cases respond so rarely to treatment with ergot that it is no longer warranted as a routine measure. Moreover, it may do harm. Modern investigations have shown that failure of such treatments is due to two causes: (1) the lack of a standard preparation of ergot; and (2) the bleeding comes from the venous side of the capillary system and is not likely to respond to treatment. Even though the drug might theoretically diminish the circulation in the uterus proper, it could not control bleeding which comes from the smaller vessels of the endometrium. Granting that ergot might excite the uterus to tetanic contractions and favor the expulsion of a polyp from its bed, there is every reason to believe that the loss of blood attending this process would more than outweigh its advantages. Practically, however, there is little use for a theoretic discussion, since ergot causes extrusions of polyps only in the rarest of cases. It does not seem worth while, therefore, to delay operation for polypoid growths, since these often may be removed by a comparatively minor operation. *Hydrastis canadensis* was formerly used by nearly all clinicians, yet the work of laboratory pharmacologists has shown that it is useless for the control of hemorrhage, a fact which had been suspected by nearly all who used it in treatment. Adrenalin occasionally is useful as a temporary measure to control the bleeding. A long list of other drugs has been used from time to time, but their very number shows that none have been specific. The only treatment by drugs which we have found of use, when the patient's condition did not demand transfusion, and we were trying to check the menstrual flow so that she might come to operation in better condition, is a combination of ergotin (grains 1), stypticin (grains 1) and hydrastinin (grains ss.) given in the form of a pill four times daily beginning the day the flow threatens.

Every patient with fibroids should be put upon a proper hygiene and diet, irrespective of plans for subsequent treatment.

Discarded Methods.—Formerly, electricity was advocated as a means not only of controlling the bleeding but of reducing the size of

the tumor. It was introduced by Tripiér, of Paris, although Apostoli was responsible for the wide vogue which it formerly enjoyed. At the present time, it has been discarded by nearly all men of experience. The reports of many commissions of societies appointed to investigate the results were uniformly discouraging save for an occasional temporary arrest of hemorrhage. This advantage was more than offset by infection which followed its use.

Curettage, like the preceding, was advocated and universally employed in the days when abdominal surgery carried a high mortality. Unfortunately, it cannot be used in the majority of cases in which bleeding is a threatening symptom, since the uterine cavity is usually distorted and the curette cannot follow its course. When the uterus can be curetted, the results are but temporary, since the endometrium regenerates in a few days, because the condition causing symptoms has not been removed.

Other measures, that is, the intra-uterine application of various drugs, as iodine, the tincture or chlorid of iron, formalin, etc., have been used and abandoned. A few years ago, atmokausis was advocated and used by a number of German clinicians. The method was followed by a few good results and a large number of complications.

Nonradical Operative Treatment.—In the early days of abdominal surgery, when the mortality attending the removal of fibroids was extremely high, various nonradical methods were advocated and practiced in cases when it did not seem wise to attempt removal of the tumor after the abdomen had been opened. Salpingo-oöphorectomy was described by Tait, in 1872, and subsequently was adopted by a large number of surgeons. Naturally, this method was attempted only in cases that did not have pelvic inflammatory disease. It secured beneficial results, probably because of the establishment of the artificial menopause, following which the tumor atrophied in the great majority of cases. At the same time, it was responsible for many distressing sequelae because proper peritonealization was impossible and abdominal adhesions were the rule. Occasionally, the arrest of hemorrhage was only temporary. Sometimes the result was delayed for many months. In other cases, the tumor did not shrink in size but continued to grow. Nor was the operation by any means as safe or as easy as an ordinary salpingo-oöphorectomy because of the vascularity of the pelvis and the extent of adhesions. Infection was common.

For these reasons, others advocated less radical measures. Schroeder and Antal practiced the ligation of the ovarian vessels and, in 1889, Rydygier tied the ovarian, uterine, and round ligament arteries, although the results were not entirely successful. In 1893, Franklin Martin proposed the ligation of the uterine vessels through the vagina, and this operation was subsequently taken up by a large number of Continental surgeons. It was found of value in tumors

no larger than an orange. With the reduction of the mortality and complications attending radical removal, these measures have been supplanted by hysterectomy.

Palliative Treatment.—This has as its object only the control of hemorrhage, since the other symptoms are not likely to respond to treatment. Our chief reliance should be placed in X-ray and radium for palliative treatment, with the idea of inducing the menopause so that cessation of bleeding will result from this cause. Other general methods should be used as adjuvant treatment, with the idea of building up the patient's general condition.

Treatment of Fibroids by Radiotherapy.—During the past 15 years X-ray has been employed extensively in Germany and frequently, although less extensively, in this country, in the treatment of fibroids. More recently, radio-active substances have been used for the same purpose. The year before the war, the literature was fairly teeming with reports of both methods and the results of treatment. The subject is again attracting widespread attention. Treatment by raying with either method may be definitely indicated in certain types of tumors, especially when the patient has systemic conditions which contra-indicate surgical procedures. The field is not wide, however, since it is not applicable to the one type of growth which is responsible for the most troublesome hemorrhage, that is, submucous growths, nor to tumors with marked degenerations, nor to those associated with definite inflammatory conditions. Since we cannot with certainty distinguish either submucous growths or early cancerous lesions, nor recognize all cases of quiescent pelvic inflammation associated with fibroids of some size, it follows that cases should be carefully selected for treatment with the rays, and the method should not be followed as a routine.

Roentgen-ray Treatment of Fibroids.—Krönig and Gauss were among the early workers who employed massive doses of X-ray in the treatment of fibroids. They recognized the need of filtration and the value of crossfire. In the years which have passed since their early work, the X-ray apparatus has become much improved. At the present time, most Roentgenologists use Coolidge tubes, with water-cooling devices, and protect the skin by aluminum filters, 3 or 4 millimeters thick. There are two methods of treatment, the intensive method, by which a single large dose is given at one sitting; and the fractional method in which several small doses are given during a period ranging from five to fifteen weeks. The interval between the treatments in the fractional method varies from one to three weeks, and is controlled by the patient's tolerance to the rays and the urgency of the symptoms. The tumor is rayed through the abdomen, and crossfire is given over the gluteal and sacral regions. The ovaries are also rayed directly. The body surface covering the pelvis is divided into a number of small

fields, each of which is treated with from 10 X to 30 X at a single sitting (X equals the erythymal unit for skin). The total dosage varies according to the size of the tumor and the technic which is adopted. The earlier workers used large doses which, however, increases the ever-present chance of X-ray burns. Krönig and Gauss, in 205 cases, used an average dose of 1480 X for a total of five weeks treatment. Steiger, in Berne, gave from 500 X to 2400 X for the five to fifteen weeks period of treatment. The majority of Americans employ smaller doses, 100 X to 500 X, since they hold that this dosage is sufficient to control the tumor and at the same time to avoid the chance of serious burns, or toxic constitutional symptoms.

METHOD OF ACTION.—There is a marked difference of opinion concerning the manner in which X-ray causes changes in the tumor. Many, among whom we may cite Meyer, Cheron, and Grafenberg, claim that there is a selective destructive action of the X-ray on the myoma cell which atrophies in consequence; and that amenorrhea does not result because of ovarian changes. Quite naturally, therefore, we should expect a more marked reduction in the size of a tumor that is composed chiefly of myomatous cells than in growths which are composed principally of atrophic fibrous tissue. It is a clinical fact, however, that hemorrhage may be arrested without marked shrinking of the tumor, and that cases presenting this phenomenon give almost without exception symptoms of ovarian insufficiency such as the flushes, and other vasomotor disturbances, soon after beginning the treatment. These findings are identical with those seen in earlier time when treatment of fibroids was confined chiefly to the removal of the ovaries without attempts to remove the tumor. For these reasons, many men believe that X-ray acts upon fibroids chiefly by killing the ovaries and inducing an artificial menopause.

INDICATION FOR X-RAY TREATMENT.—The age of the patient is often an important consideration when selecting a suitable type of treatment. X-ray is not the method of choice in women of thirty-five, or less, since the treatment is very likely to be followed by a permanent amenorrhea. If the preservation of ovarian activity is an important consideration, the use of X-rays appears to be contra-indicated, although some, as Frank, and Pfahler, feel that by proper dosage, the tumor may be reduced without hurting the ovary to the extent that subsequent pregnancy is impossible. Intramural tumors occasioning hemorrhage are most favorable for the employment of X-ray, in the absence of pronounced degenerative changes or adnexal inflammation. It is generally agreed that submucous or subperitoneal fibroids, and cervical and broad ligament tumors are better treated by surgery. It is a fact, however, that by the ordinary clinical methods of examination, we cannot differentiate between interstitial growths and certain forms of submucous tumors. The size of the tumor is also an important consideration. Fibroids reaching to the level of the umbilicus are so often associated with degenerations and complications that the employment of X-ray should be restricted

to tumors which occupy the pelvis of women approaching the menopausal age, or those in whom there are definite contra-indications to surgery. The fact that adenocarcinoma of the body of the uterus occurs so frequently with fibroids (at least 2 per cent of cases) demands the exclusion of this complication before X-ray treatment is attempted.

CONTRA-INDICATIONS.—Incarcerated tumors, submucous or subperitoneal growths, evidence of gangrenous and suppurative processes, the presence of adnexal disease, or suspected malignancy, contra-indicates its employment. A rapidly growing tumor is usually associated with either a benign or a malignant degeneration, and surgical removal in these cases is better judgment. We have frequently emphasized that it may be impossible absolutely to diagnose the presence of complications. This is well shown by many reported cases. Vineberg, in 1915, reported a multipara of 28 presenting a fibromyoma associated with an adenocarcinoma, the only symptom of which was prolonged menstruation. Personally, we have seen several such cases in women of more mature years (see Figs. 32 and 36). Mackenrodt, in 1912, reviewing 418 fibroids treated surgically, claimed that only 21 might have been treated properly by X-ray. Tracy, in 1915, studying 3,561 fibroid operations, felt that there were definite contra-indications to raying in 33 per cent and that 14 per cent would have died if that were the only form of treatment. Erdmann, in 1917, reported 330 hysterectomies for fibroids with but two deaths (6 per cent mortality). Ten of the cases in this series presented malignancy, together with the fibroid so that, had X-ray been used in all the cases, there would have been an absolute mortality from unrecognized malignancy alone of 3 per cent.

RESULTS OF X-RAY TREATMENT.—The results are usually expressed in terms of cure of the symptoms. Occasionally the size of the tumor is mentioned. Krönig and Gauss, in 1913, published the results of their treatment of 205 cases of fibroids. They state that the methods was applicable to 85 per cent, and that a symptomatic cure was obtained in 100 per cent. They did not regard adnexal disease as a contra-indication, and claimed that the nervous symptoms were less marked because the internal secretion of the ovaries was still preserved. Frank, on the other hand, felt that only 5 per cent of his series of fibroid cases should be treated with X-ray. Eymer, in 1912, reported the results of the treatment of 94 cases of fibroids in Heidelberg. Amenorrhea was obtained in 49 cases and a distinct reduction of the size of the tumors was noted in 30 cases. Steiger, in 1915, reported his results for 23 cases which ranged in size from a man's fist to a man's head. Symptomatic cure was produced in 85 per cent. Mohr collected from the German literature 796 fibroids which were treated by X-ray. At the time of the report, 127 were still under treatment, or had been lost to view, so that his report was based on the study of 669 cases. Of these, 376, or 56.2 per cent, were considered cured. Amenorrhea was produced in 97.1 per cent of this group. Oligorrhea was produced in .8 per cent. In 2.1 per cent, there had been no complaint of menorrhagia. Of the 669 cases, 120, or

17.9 per cent were improved. In 37.5 per cent of these, amenorrhea was desired but was not obtained, although oligorrhea resulted in the majority. Normal menstruation was produced in 10.8 per cent and improvement as far as hemorrhage was concerned, resulted in 51.7 per cent. In this series,

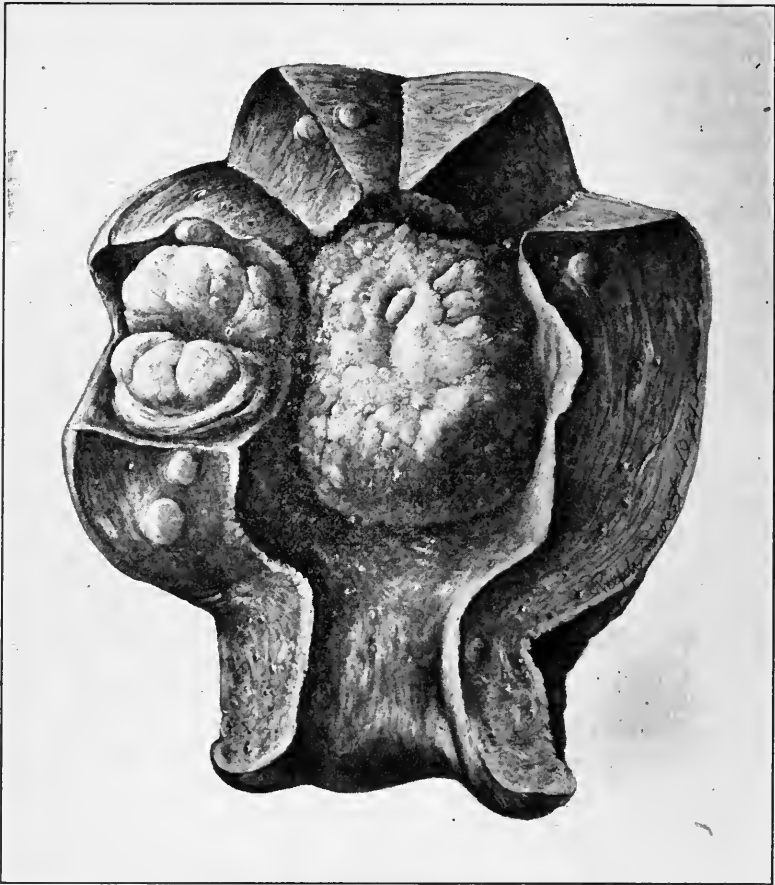


FIG. 36.—ADENOCARCINOMA OF FUNDUS WITH FIBROIDS.

11.1 per cent were not cured; recurrences occurred in 1 per cent and deaths in .29 per cent. His table is of interest and is given below.

RECORD OF 202 FIBROID PATIENTS

Age	Number cases	Per cent		
		Cured	Improved	Not cured
30-40	28	46.4	42.9	10.7
40-50	131	80.9	10	9.1
Over 50	43	93.8	4.7	2.3

SIZE OF TUMOR IN 380 CASES

	Per cent
Unaltered	21.3
Reduced	57.6
Markedly reduced	13.7
Entirely disappeared	5.3
Subjective sensation of diminution.....	.8
Increased	1.3

Brettauer, in 1918, reported the results of 33 fibroids treated by him with X-ray. Permanent amenorrhea occurred in 78 per cent and temporary amenorrhea in 22 per cent. The tumors had varied in size, some reaching up to the umbilicus. In almost every case, he found a decided reduction in size and, in some cases, the tumor entirely disappeared. Beclere, in 1920, recorded his results for 400 cases. Of these cases, 25 per cent were over fifty years of age; 11 per cent were under forty; and 64 per cent were between forty and forty-nine years. The size of the tumors was indicated by the fact that 85 per cent of them were palpable through the abdomen before treatment. He used the fractional method of dosage. The hemorrhage was controlled in 60 per cent of cases by twelve to fourteen weekly treatments. A menopause was produced in these 60 per cent, although in 12 per cent the periods were suppressed only temporarily and returned after a few months or years. Beclere states that the growth of the tumor was arrested in all cases and was usually diminished in size. Martindale, in 1920, reports the results of X-ray treatment in 37 cases. Amenorrhea was produced in 30 of these and was not produced in 5. The other 2 cases already had amenorrhea. The number of treatments necessary to produce amenorrhea is of some interest; two treatments sufficed in 6 cases; three treatments in 6; four treatments in 11, although in one of these the periods returned at ten months and were then checked by two other treatments; five treatments were necessary in 6 cases, although normal menstruation returned in 1 of these after seven months; seven treatments were necessary for 1 case.

Amenorrhea was not produced in 1 case after five treatments, although normal periods resulted. It also failed in cases that were treated seven, eight, nine, and twelve times without stopping the bleeding. One case had had amenorrhea for three years before treatment. The tumor was not reduced after nine treatments. The growth was reduced to half its former size after six treatments in 1 case; after seven, in 2 cases; and after eleven, in 2 cases.

Personally, we see several cases each year in which it is necessary to remove growths which do not respond to treatment. On the contrary, we occasionally see astonishingly good results. It is unfortunate, however, that the literature does not indicate the frequency of

burns which have formed such an unpleasant and troublesome complication.

Radium Treatment of Fibroids.—The physics, method of screening, and methods of application have been described under radium (q. v., p. 120).

INDICATIONS.—Indications may be afforded by fibroids which cause bleeding in women of more than thirty-five who have comparatively small tumors, or in younger persons in whom a previous myomectomy has been followed by recurrence of the tumor. Just as in treatment with X-ray, the best results are to be expected when the tumor is of the interstitial form. It is extremely important that cases be selected properly for treatment, since all fibroids should not be treated as a routine, either by surgery, X-ray, or radium. Tumors the size of a three-months pregnancy, or smaller, when properly selected, respond well to radium. The hemorrhage ceases, or is controlled, and the growth shrinks in size when the treatment is well chosen. There is no evidence to justify the belief that large fibroids giving pressure symptoms should be treated in this manner.

CONTRA-INDICATIONS.—The chief contra-indication is offered by the presence of old pelvic inflammatory disease. Cases in which this condition is suspected should never be selected for radium treatment, since it may light up the old process and cause a peritonitis. Deaths from this cause have been reported. Submucous and subserous tumors do not react well to this method. This is extremely unfortunate since, as has been repeatedly stated, submucous fibroids are responsible for the great majority of fibroid cases presenting severe and protracted bleeding. The method should not be attempted in any case in which degenerations are even suspected, since radium does not convert such tumors into fibrous connective tissue, but increases the extent of the degeneration and favors the absorption of toxic products which may give severe symptoms. Death has occurred in such cases and Clark emphasizes the fact that such a patient may serve as "a sarcophagus for her decadent tumor."

While carcinoma of the uterine body does not contra-indicate the use of radium, it is a fact that such cases do better with surgical procedure. The condition can be diagnosed with certainty, since the careful man cures the uterus immediately before inserting the radium. If he studies his curettings, the condition cannot remain unsuspected. The presence of sarcomatous degenerations in the fibroid tumor does not offer a contra-indication, since such growths react favorably to radium. The condition may not be diagnosed, since sarcoma of this type does not early invade the endometrium. Tumors with calcareous degenerations do not react to the treatment.

The contra-indications for radium treatment of fibroids has been summarized by Clark as follows:

1. Tumors larger than a three- or four-months pregnancy should not be rayed unless there are decided surgical contra-indications, such as serious heart lesions, diminished renal function, or other constitutional defects which could render an operation a serious procedure.

2. All tumors associated with symptoms indicative of inflammatory lesions, because of the many reported cases in which a flare-up of an old inflammatory lesion has formed a most distressing complication following radium.

3. Patients with normal or slightly increased menstruation who present a cachectic appearance and toxic symptoms out of all proportion to the amount of hemorrhage. This type of case usually indicates well-marked degenerations of the tumor.

4. All cases in which there are symptoms of coexistent abdominal lesions, such as symptoms of cholecystitis, appendicitis, etc.

In spite of these numerous contra-indications, excellent results will follow the radiation of cases that have been properly selected, that is, tumors of small size with hemorrhage as the chief symptom, occurring in middle-aged women, without any evidence of extensive degenerations.

METHOD OF ACTION.—In contrast to the X-ray, radium in proper dosage acts chiefly on the tissues of the uterus and the tumor which it converts into fibrous tissue. The action on the ovaries is less marked and, with properly controlled treatment, the ovarian function need not be injured. The tumor is reduced in size in nearly all cases.

TECHNIC.—The technic is identical with that for a curettage. The labia are shaved and the vagina is cleaned with soap and water, $\frac{1}{2}$ per cent lysol solution, and 60 per cent alcohol. It is not necessary to catheterize if the patient voids. The rectum should be emptied with an enema several hours before the operation. Anesthesia is usually necessary. Nitrous oxid and oxygen meets all indications. The cervix is exposed by means of vaginal specula and is grasped and steadied with a tenaculum, while the cervix is dilated to admit the capsule containing the radium. The uterus is then curetted, and the tissues which have been removed are carefully inspected to be sure that carcinoma is not present. The radium is then inserted. It may be used either as a salt or emanation. The arrangement of the capsule depends largely upon the size, length, and position of the uterine cavity. In general, the radium should be applied over as much of the uterine surface as seems feasible. Four tubes of radium mounted tandem in suitable capsules of brass or silver, sufficient to exclude the majority of the Beta rays, will suffice for the largest tumors in which treatment is indicated. Ordinarily, two bars suffice. They should be included in a heavy tube of black rubber and inserted directly into the uterus. The vagina is then packed with gauze.

DOSAGE.—The dosage depends upon the age of the patient and whether

a menopause is desired or menstruation is to be preserved. While not definitely standardized, women under thirty-five should have about 400 mg. or mc. hours for their initial dose. It is better to give too small rather than too large a dose at the first treatment. Women thirty-five or more, may be given a larger dose at the first treatment; 50 mg. or mc. for twenty-four hours meets with the approval of the majority of workers. We see no objection to giving 100 mg. or mc. for twelve to fifteen hours.

RESULTS.—Kelly, in 1914, reported his results with the radium treatment of 21 fibroids ranging in size from a two-months pregnancy to growths as high as the umbilicus. The ages range between thirty-three and fifty-nine years. The tumor shrunk in size or disappeared in each case and complete amenorrhea was obtained in 16 cases. He was unable to insert the radium in the uterus in 1 case which could not, in consequence, be treated. In 1918, Kelly reported his results for 211 cases of uncomplicated fibroids of varying size. In this series, 87 women were cured and the tumors disappeared or became insignificant in size. Fourteen were well but failed to report for subsequent examination. The tumor reduced in size in 62 cases but since two years had not elapsed since the last treatment, the investigator felt the interval was too short to draw any conclusions. Two cases presenting complications were not improved by the treatment. Eight did not stay cured and were subsequently operated. There were 2 deaths following treatment. His method consisted in the application of from 300 to 500 mcs. maintained in place for three hours.

Stacy reports a series of 600 cases treated by radium at the Mayo Clinic. She divides the material into two classes, according to their age. There were 122 women under thirty-five of whom 19 were twenty-five or under. Small initial doses were given to these, aiming to control the symptoms but not to stop menstruation. The average dose for this group of cases was about 300 mg. hours. Menorrhagia was controlled by one treatment in 55.6 per cent of cases. A second treatment was necessary in 17 cases. A larger dose was given to the women of thirty-five and over, although it must be classed as small. In 349 patients, a second treatment was necessary in 64 and a subsequent operation was done in 20. Curtis, in 1920, briefly summarizes his results in the treatment of 62 fibroid tumors in which 50 mgs. of radium were applied for approximately twenty-four hours. He states that the hemorrhage always stopped but that the decrease in size of the tumors varied considerably. Subsequent hysterectomy was necessary a few times because of symptoms from preëxisting pressure or adhesions. This series comprises selected cases in which the tumors were of small size and which gave symptoms of hemorrhage. Clark, in 1920, states that in a series of over 150 cases selected for radium treatment, the results in 4 were not sufficient to satisfy them, or him-

self, and he subsequently did a hysterectomy. Two others were operated on at other clinics. In all others, the results were most satisfactory and recovery ensued without complications in all except one.

Radical Treatment.—There is not yet complete agreement as to the extent to which radical treatment should be employed. The view that we should remove all fibroids unless there are contra-indications to surgical treatment is combated by many excellent results which have been obtained by treatment with X-ray or radium. It is a fact, however, that no treatment which has yet been advanced is completely free from mortality, even X-ray or radium. Malignant degeneration occurs so frequently in cases where its presence has not been even suspected that the physician should bear in mind the fact that the removal of the uterus and tumor alone offers absolute chance of cure. The advocates of operation in all cases call attention to the point that the removal of small tumors is attended with a very small mortality, while that of the larger growths is very low in proportion to the size of the tumor. The opponents of this view state that the mortality from non-operative treatment (X-ray and radium) is much less than that following operation and believe that the indications for removal should be restricted only to growths which are causing symptoms and in which the tumor is large and rapidly growing. The common sense of the matter is that cases should be considered individually for the various treatments. Large growths in comparative youth should be removed early while small growths in women approaching the menopause may properly be treated with X-ray or radium, if the diagnosis of malignancy has been absolutely excluded. The fact that fibroids may kill has been shown in the section on prognosis without operation (see page 171). Even if we grant that the figures of Noble and Winter are too high for present consideration, since they represented conditions which obtained before fibroids were removed early, we must admit that fibroids may kill through degeneration, and that many women escape this danger only to undergo invalidism. The surgeon must be guided in his treatment by his results and by the mortality which follows his own treatment. Nearly all now recognize that good results cannot be obtained by emergency operations *in extremis* and that a proper surgical technic has been developed so that operations may come into competition with nonsurgical measures.

POSITIVE INDICATIONS FOR OPERATION.—The more important degenerations indicate operation in cases presenting symptoms, or in tumors of considerable size without symptoms. Olshausen, a generation ago, stated that degenerations do not occur in more than 5 per cent of cases, yet the careful work of Winter has shown that sarcoma alone occurs in nearly 5 per cent of growths of average size. The frequency with which carcinoma occurs with fibroids is emphasized by nearly all recent investigators. If one observer, as Winter, has proved that malignancy

occurs in 5 per cent of cases, it is useless to cite a long list of authors whose proportions of malignancy are smaller, especially if we know that the routine examinations of many of the series could be subjected to criticism. Hemorrhage that does not respond to other measures demands operation before the patient's chance is impaired by the sequelae of marked anemia. The large number of serious secondary complications in the adnexa and the actual presence of a growing tumor form indications which cannot be disputed. Yet one should carefully review the various factors of age, social state, and other similar points before deciding in favor of an operation which is not demanded by conditions which threaten life or promise invalidism. We should bear in mind, however, if the case be elected to wait for the menopause, that this condition is usually greatly postponed in fibroid cases even well into the middle of the fifth decade, even in tumors of comparatively small size. The physician who does surgery only occasionally should remember that there is always mortality attending the removal of fibroids, and that it is likely to be much greater in his hands than in those of an expert. Primary operations are not practiced by most conservative men in more than 50 per cent of the cases which come under his observation.

CONTRA-INDICATIONS TO OPERATION.—These are the same as for any other surgical procedure. No operation should be undertaken unless the patient has been subjected to a most careful routine examination in which all necessary tests are made to establish the function of the heart, lungs and kidneys. Anemia may offer a contra-indication. We do not operate cases with hemoglobin of less than 50 per cent until they have been treated with blood transfusion.

The *surgical procedures* at the present time are *myomectomy* and *hysterectomy*, and there has been much discussion as to the relative advantages of each. There is no doubt but that, from the standpoint of pure theory, myomectomy has many advantages of a conservative nature if done on young women. For example, it leaves them often able to bear children and avoids the induction of an artificial menopause, which so often entails many distressing nervous complications. It should not be performed on women more than thirty-five years of age, since experience has shown that secondary operations are often necessary subsequent to myomectomy. It should be the surgeon's aim to accomplish all that is necessary at a single operation. Myomectomy does not seem justifiable if there are multiple fibroids of large size imbedded in the uterus. There is always a question as to what the scar will stand in case of subsequent pregnancy. Tubal or ovarian disease also contra-indicate myomectomy as does any other condition which is a barrier to pregnancy. Myomectomy should not be attempted if the growth is of large size, because of the considerable chance of malignant changes. Moreover, the removal of the larger tumor in no

way interferes with the development subsequently of the smaller growths which may be so readily overlooked at time of operation. Quite to the contrary, in fact, since the latter grow frequently to considerable size because of the improvement in the uterine circulation following myomectomy and occasionally demand removal by secondary operation. Finally, multiple myomectomy may be contra-indicated when it appears impossible satisfactorily to peritonealize the numerous incisions. If surgery is to be used for the treatment of chronic conditions which do not uniformly kill, the operator must see that his technic does not excite secondary symptoms more severe and dangerous than those which constituted the first complaint.

The older literature shows that myomectomy was followed by a mortality greater than that attending hysterectomy. Hunner, in 1903, reported a mortality of 5 per cent in 100 cases of myomectomy in Kelly's clinic. Winter, in 1904, compiled 451 cases of Hofmeier, von Rosthorn, Martin, Olshausen, Schauta, and Zweifel and found a mortality of 9.8 per cent in contrast with a 4.5 per cent mortality of a large series which the same men had treated by supravaginal hysterectomy. Kelly, in 1907, reported a mortality of 4.5 per cent for 306 myomectomies in contrast with the mortality of 3.1 per cent for 691 hysterectomies. Kelly and Cullen, in 1909, give a mortality of 5.4 per cent for 296 abdominal myomectomies. Fifty per cent of these deaths were caused by intestinal obstruction, peritonitis, or both. Subsequent operation was necessary in 18 of the 280 cases who survived the primary operation. The same authors obtained a mortality of 6 per cent in 84 vaginal myomectomies. They followed 48 of their surviving cases and found that subsequent hysterectomy was necessary in 2 of them and that carcinoma developed in 1 other. The primary mortality for their series of 901 abdominal hysterectomies was 5.5 per cent and no mortality in 24 cases treated by vaginal hysterectomy. The earlier cases of the series were responsible for comparatively high mortality, since the cases operated for two and a half years before the report were done with less than 1 per cent mortality.

These figures give the mortality of an older period. With improvement of technic, better conditions obtain. Bad results were often reported when myomectomies were done for large tumors. This may have been due to tying too tightly the sutures which effaced the cavity caused by the removal of the tumor. There is a striking resemblance between the uterine muscle which has hypertrophied in response to the stimulus presented by a fibroid tumor and the uterine musculature in pregnancy. Just as in cesarean section, we must expect some bad results in myomectomy, since the sutures are placed in a uterine musculature which is undergoing involution. Bad results follow improper peritonealization. The illustrations in textbooks show this in a striking way; a row of knots with the long ends of catgut projecting beyond

the peritoneal surface of the uterus is invariably shown. Nature always covers these surfaces with adhesions. A proper peritoneal cover is shown in Fig. 40 (q.v.).

During the last few years, it has been conclusively proved that myomectomy should carry a risk no greater than that of supravaginal hysterectomy. Mayo, in his report in 1910, gave the mortality of 2.3 per cent for 1,244 myomectomies in which 820 coincident operations were done. The mortality for 900 supravaginal hysterectomies was 2.3 per cent. Essen-Moeller, in 1917, obtained nearly identical percentages of death in myomectomy and supravaginal hysterectomy. Mayo, in 1917, reports 504 consecutive myomectomies with four deaths (0.8 per cent). Five of the cases required subsequent hysterectomies. Recent literature indicates that the mortality attending surgical treatment of fibroids is now well under 2 per cent. Deaver, in 1916, reports 750 cases operated with 1.73 per cent. Broun, in 1918, records 1,500 cases treated surgically with 1.8 per cent mortality. There were 262 cases operated at the Woman's Hospital in New York during 1918, with 4 deaths (1.5 per cent).

Myomectomy.—Myomectomy may be performed through an abdominal or vaginal incision. Unless there are compelling reasons why the vaginal route should be used, the method of choice is through an abdominal incision.

Preliminary to either method, the vulva should be shaved and the vagina washed out, with soap and water, lysol and 70 per cent alcohol. In case the operation is to be done through the abdomen, the vagina should be packed with a long strip of sterile gauze.

ABDOMINAL MYOMECTOMY.—There are a number of points in technic which merit especial consideration. The exposure should be adequate, so that the work may be done in place and without forcibly dragging the uterus out of the abdominal incision. The surgeon should avoid all unnecessary trauma, since the subsequent health of the patient will be largely determined by the presence or absence of abdominal adhesions following operation. In this connection, it may pay to review certain errors in the usually accepted technic. Many men routinely suture the peritoneum to the skin in order to limit the bruising of the abdominal fat during the operation. The peritoneum is infinitely more sensitive to trauma than is the fat, and injuries resulting from bruising it entail far more serious consequences. The flap of the peritoneum that is pulled up to the skin must suffer serious abrasions from the tugging of the retractors and the handling that is necessary in all abdominal operations. At the end of the operation, these abraded areas are usually turned back into the abdomen and are not made extraperitoneal in closing the peritoneum. Adhesions of the omentum or bowel almost uniformly result. There is also the very great possibility that the visceral peritoneum is injured by the abdominal packs which are used



FIG. 37.—ABDOMINAL MYOMECTOMY. Fixing the tumor. (Doederlein-Krönig.)

to hold back the intestines from the field of operation. Any gauze, even though wet, will cause the denudation of the delicate peritoneal cells. At the close of an hour's operation, one may see the imprint of the gauze mesh upon the bowel peritoneum. There is also an enormous intraperitoneal extravasation of serum. Our experience has shown that a large, heavy rubber dam is less irritating than the wet gauze packing and is to be preferred for that reason.

There is also much to say as to the type of the incision. In our minds, nothing equals the midline incision, since you cut through a minimum of nerves and vessels and have the best opportunity of obtaining a firmly closed incision. Especially is this true if the median edges of the recti muscles are turned from their sheaths to create broad areas for apposition. Many surgeons advise an incision in the mesial edge of the rectus muscle. This, in our judgment, is an error. Nearly all women who have borne children have a diastasis of the recti which frequently amounts almost to a hernia. The diastasis cannot be closed if one uses a rectus incision. The nerves of the muscle are also severed by the rectus incision and are far more likely to favor the production of abdominal adhesions as has been shown by the experimental work of Sweet, Cheney and Wilson. These observers found that definite mechanical trauma, such as scrubbing the peritoneum underlying the rectus muscle in dogs, was not uniformly followed by firm bands of adhesions except when the abdominal approach was made by a rectus incision and the consequent injury of nerves of the abdominal wall.

Fixed mechanical abdominal retractors are far better than the hand retractors, since, when they are locked, they hold the edges firmly apart, and cannot move to and fro to cause peritoneal abrasions as must the hand retractors which are held by assistants. Nor do the edges of the blades impinge in the neighborhood of the vessels of the abdominal wall to traumatize and favor thrombosis and embolism as the hand retractors always do.

The *technic of abdominal myomectomy* depends largely upon the site and form of the growth which is to be removed.

TECHNIC IN SUBPERITONEAL PEDUNCULATED FIBROIDS.—The growth is seized by a tenaculum and an incision is made through the peritoneal covering at the uterine margin of the pedicle. The peritoneum is then stripped backward as a cuff and the exposed base of the pedicle is sutured as may be necessary to control all bleeding with one or two plain catgut sutures. The tumor is then cut away externally to the ligatures. When the tumor has a broad, pedicled base, one should plan the incision so that there results a craterlike cavity after the tumor is removed, which can be closed without tension by a continuous running plain catgut suture placed deeply. The peritoneal cuff, after the removal of either type of tumor, is inverted and closed with fine No. 00 plain catgut mounted on a curved intestinal needle, so that there is no

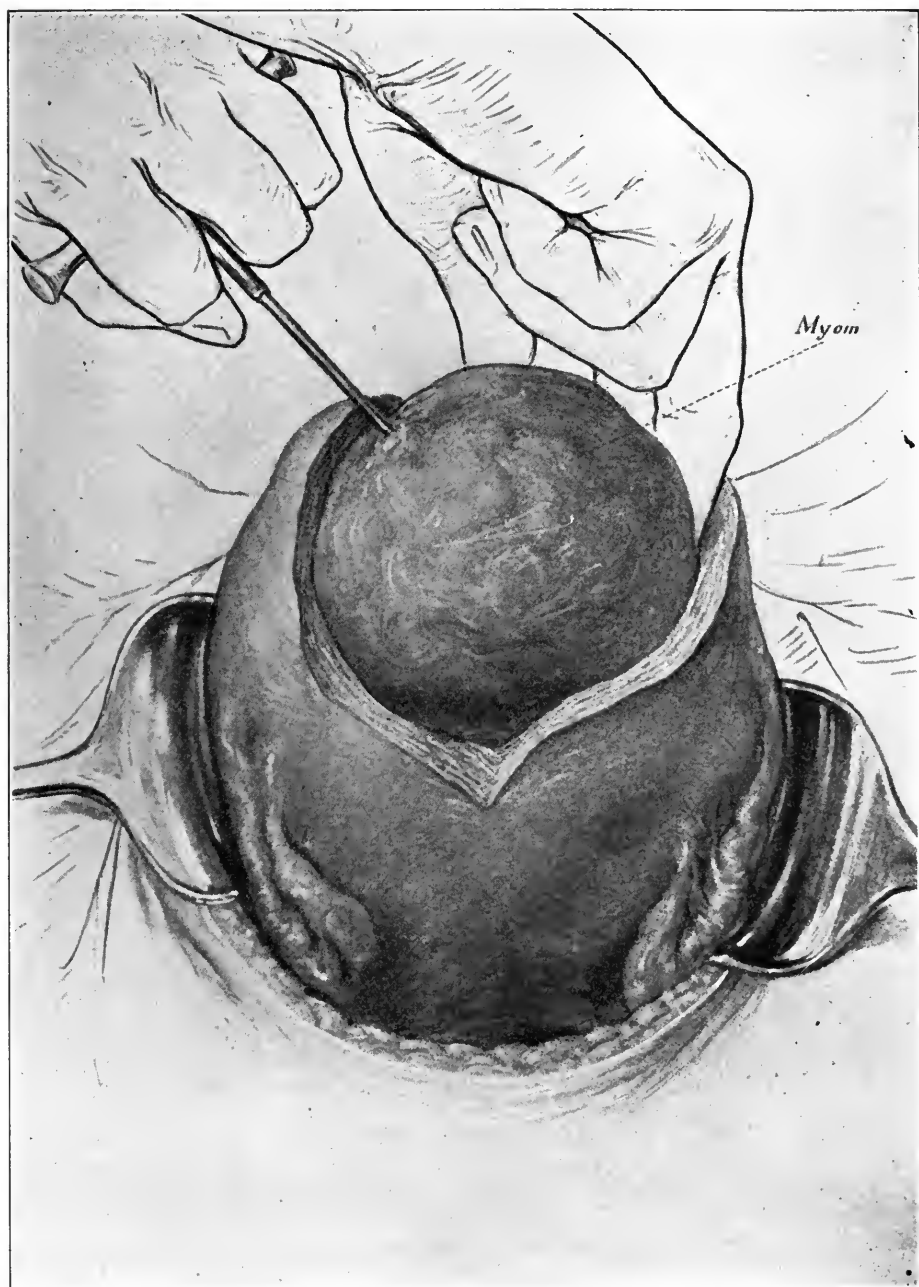


FIG. 38.—ABDOMINAL MYOMECTOMY. Shelling out the tumor. (Doederlein-Krönig.)

exposure of any raw surfaces and only the final knot lies upon the serous surface.

TECHNIC IN SUBPERITONEAL SESSILE AND INTERSTITIAL FIBROIDS.—When there are a number of growths to be removed from the uterine body, the incision should be planned so that they shall be as few as possible and shall run in the same direction. The incision is then made



FIG. 39.—ABDOMINAL MYOMECTOMY. Closing the cavity in layers to secure perfect approximation,

through the capsule until the tumor or tumors lie exposed. The growth is now seized with a tenaculum and the opening in the capsule is enlarged sufficiently to allow the removal of the tumor (Fig. 37). The tumor is separated from its bed by blunt dissection, which usually occasions no difficulty (Fig. 38). Very rarely it may be necessary to cut it with scissors. One should exert every care so that the uterine cavity will

not be opened. In case there is much hemorrhage, the margins of the uterine wound are widely retracted with narrow retractors or by single tenacula. Any bleeding vessels are transixed and tied with ligatures mounted on small needles. The raw bed of the fibroid is now closed without tension by continuous No. 1 plain catgut sutures (Fig. 39). The peritoneal edge of the incision is inverted with a No. 00 plain catgut suture

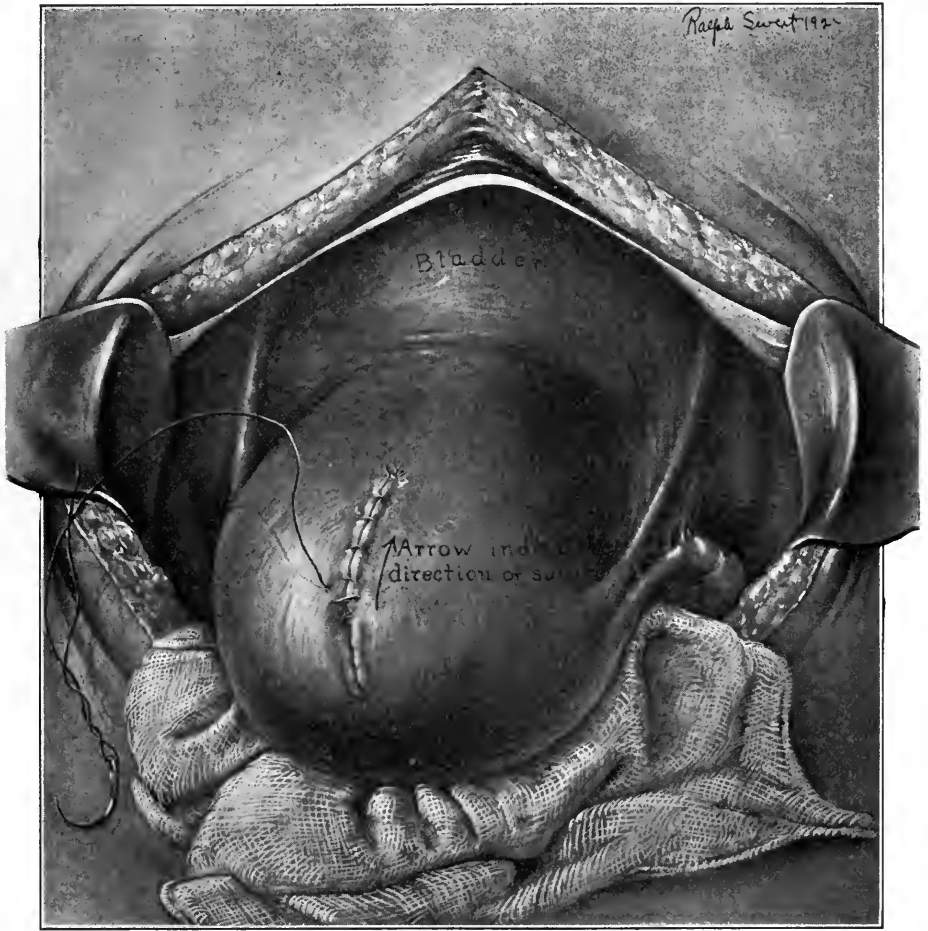


FIG. 40.—ABDOMINAL MYOMECTOMY. Proper peritonealization obtained by approximating the serous surfaces with fine plain catgut sutures

mounted on an intestinal needle (Fig. 40). Very rarely there is considerable hemorrhage from the bed of the tumor. If this cannot be checked by hot packs, it is usually controlled by figure 8 sutures tied only as firmly as is necessary to arrest the bleeding. It is not well ever to tie sutures in myomectomy operations tighter than is absolutely necessary, since they readily cut through after the closure of the operation. If the hemor-

rhage cannot be checked in this manner, an assistant should make pressure on the cardinal vessels to stop the bleeding.

This operation may be employed in cases which have several fibroids in the uterus lying close together. Yet multiple myomectomy is not usually advisable, since it is extremely likely that other fibroids not exposed to view may develop after the operation and later present their symptoms. Very large fibroids, even when single, should not be removed by myomectomy, since a good closure cannot always be obtained without extreme distortion of the uterus. Myomectomy should never be performed if there is chance that the uterine cavity is infected. The patient may lose a considerable amount of blood during a myomectomy for a large growth, and the uterus is not likely to be a satisfactory organ if pregnancy should subsequently result.

Very rarely it may be found advantageous in performing myomectomy to split the uterus in halves at the beginning of the operation, cutting down directly through the tumor. The edges of the wound are then widely separated and the divided growth is shelled from out its bed. This method is preferable to the former in difficult cases, and especially in those in which the uterus is impacted in the pelvis. Nearly all operators, however, advocate a supravaginal hysterectomy in cases requiring so great a wound in the uterine muscles.

TECHNIC IN INTRALIGAMENTOUS FIBROIDS.—Myomectomy is suitable only for growths that are so small that they can be removed with little bleeding and trauma. Large intraligamentous tumors should not be removed in this manner unless the pedicle is very small. When these tumors present complicated relationships with surrounding structures, as is usually the case, hysterectomy is the method of choice. There is apt to be less bleeding after hysterectomy than after myomectomy, and far less chance of injuring the ureters and pelvic veins. When the tumor has been dissected from the areolar tissue, the incision should be covered by the excess of loose peritoneum, so that there may be smooth peritoneal surfaces and no displacement from the normal uterine position. The round ligaments often can be utilized for making a smooth peritoneal covering and for holding the uterus in place.

VAGINAL MYOMECTOMY.—Vaginal myomectomy is often advocated by surgeons who have safely removed large tumors through the vagina. Yet, as a rule, the results which they have obtained merely demonstrate the possibilities of the operation, not its relative desirability. Since the operative technic of the abdominal operation has become fairly standardized, the removal of large tumors is more safe through the abdomen than through the vaginal orifice. Vaginal myomectomy is preferable for the removal of tumors which present in the uterine cavity, especially for submucous fibroids which have become infected. There are numerous reports in the medical literature of tumors weighing as much as six or eight pounds that have been removed by this

means. The usual limitation of size is that of the fetal head, or roughly speaking, a tumor 10 or 12 centimeters in diameter. Such growths, however, should be reduced in size if they are to be removed without great trauma.

Vaginal myomectomy is indicated for the removal of (*a*) small fibroid polyps contained in the cavity of the uterus or projecting through the cervical canal down into the vagina; these usually cause little difficulty and can be snipped off with the scissors; (*b*) larger submucous fibroids which are contained in the cavity of the uterus or undergo expulsion into the vagina, especially when they are single and not of great size; these growths are usually infected and removal should not be attempted until the field of operation has been disinfected in a satisfactory manner by a rather extended period of local treatment with irrigations, unless hemorrhage and anemia are prominent symptoms.

Vaginal myomectomy may be used to remove (*c*) cervical fibroids of moderate size which can usually be reached after exposure has been obtained by colpotomy or hysterotomy; (*d*) subperitoneal fibroids of moderate size which are situated on either the anterior or posterior wall; (*e*) single intramural fibroids of moderate size, especially when situated on the anterior wall.

Indication may be afforded in fat women because of their size, although, as a rule, the last three groups of tumors are removed more satisfactorily after laparotomy, since proper peritoneal cover can be made in a better manner.

TECHNIC IN PEDUNCULATED SUBMUCOUS FIBROIDS.—The tumor may be removed through the dilated cervix, or after the cervix has been split by means of a hysterectomy. The latter is the method of choice in case the polyp does not project through the external os.

A tumor which projects through the dilated os is seized with the forceps and twisted off from its attachment, or else its pedicle is snipped with the scissors. This should not be attempted until the condition of the growth and its pedicle has been ascertained by inspection or careful palpation, since malignant changes, unfortunately, are common. The cavity of the uterus is then packed after it has been swabbed with half tincture of iodine. The pack is removed in twenty-four hours.

If the polyp does not project through the external os, the tumor may be removed in a similar manner after exposure has been obtained by hysterotomy. At a rule, the anterior hysterotomy is preferable. The cervix is seized by its upper central margin with two tenacula, and an incision is made on the anterior vaginal wall transversely and below the level of the bladder. The bladder is now separated from the cervical wall as high as the level of the internal os by means of dissecting scissors. The anterior lip of the cervix is now divided in the midline. As a rule, the incision bleeds but little and the oozing can readily be controlled by traction of tenaculae applied to each side of the in-

cision. In the same way, the uterus is brought down and into view. If the tumor is of comparatively small size, it may be removed without reduction of its size. Larger growths should be reduced in size by a method shown in Fig. 41. When the pedicle is reached, it may be ligated and divided with the scissors. Torsion is frequently helpful in controlling the bleeding. The pedicle should not be divided too close

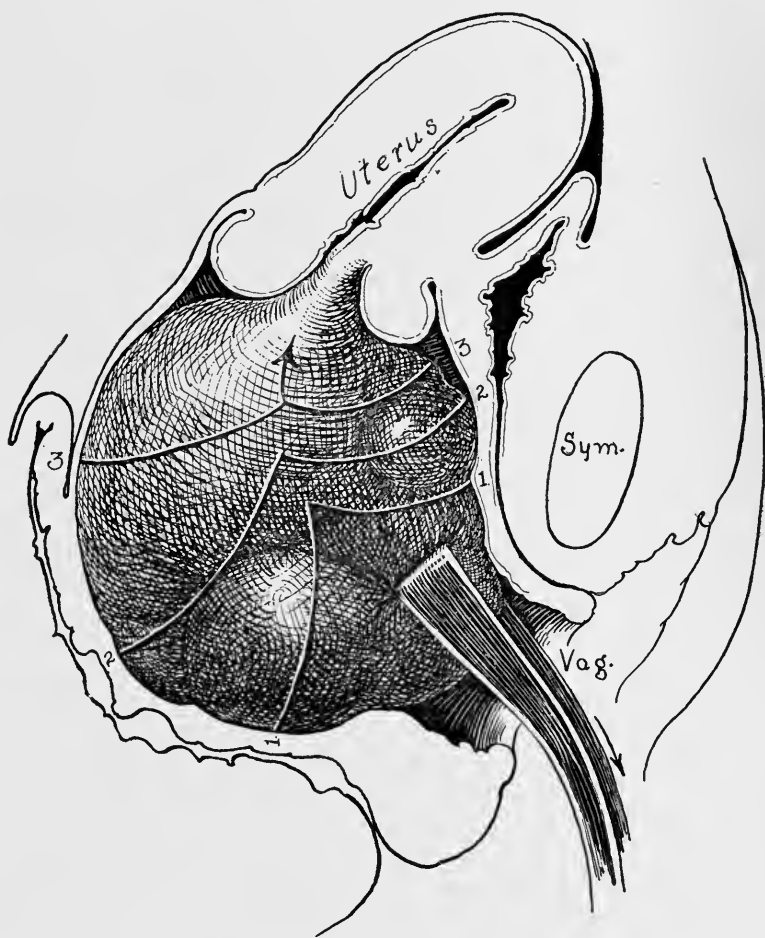


FIG. 41.—VAGINAL MYOMECTOMY. Incisions for reducing the bulk of the tumor.

to the wall, since the uterus often prolapses with the tumor and the incision unwittingly may extend well into the uterine body. As in the previous operation, the abraded area should be swabbed with half tincture of iodine and packed after the wound has been closed with interrupted No. 2 chromic sutures. There is no need of drainage under the bladder.

TECHNIC IN NONPEDUNCULATED SUBMUCOUS FIBROIDS.—The indications for myomectomy in this group of tumors are comparatively few,

since experience has shown that they are far better treated by hysterectomy. As in the previous case, a hysterotomy is made in the anterior wall of the uterine cervix and the bladder elevated out of harm's way. When sufficient exposure has been obtained in this manner, the prominent portion of the growth is seized with a tenaculum and an incision as long as possible is made through the mucosa and the capsule of the fibroid. The tumor is then shelled out with the fingers or the scissors, being drawn down gradually with forceps as it is liberated. The larger tumors are best removed after morcellation. Yet, as emphasized before, this class of tumor is often infected, and it is not wise to leave the uterus, since the convalescence at best may be stormy. Hemorrhage is likely to occur and may not respond to packing. The treatment is not advised, save in the very rarest cases.

TECHNIC IN INTERSTITIAL FIBROIDS.—The removal of fibroids of this class by morcellation is an obsolete procedure, and, therefore, does not merit description. It is mentioned merely to condemn it. If this type of operation appears necessary, the uterine arteries should first be ligated. In closing, care must be taken so that the peritoneum which has been reflected above the abraded areas is sutured above the former location of the tumor. This type of case is far better treated by radium.

TECHNIC IN SUBPERITONEAL FIBROIDS.—Subperitoneal fibroids may be removed when the vagina is capacious and the primary operation is designed only for the repair of the pelvic floor. There is no contra-indication to removing growths of small size which are situated upon the anterior surface of the uterus, since the incision required for the myomectomy may be covered by the bladder. There is considerable risk of adhesions to the small bowel if the myomectomy is made upon the posterior surface of the uterus, since one cannot well judge as to the hemostasis when the uterus has been inverted through a colpotomy incision into the vagina.

The cervix is steadied with tenaculæ and a transverse incision is made into the anterior vaginal wall below the insertion of the bladder. If the growth is high, or of appreciable size, a vertical incision should be made so that the bladder may be completely elevated. The separation is made with the dissecting scissors. When the bladder is well elevated by a broad retractor, the peritoneum is incised, the fundus seized, and the uterus inverted through the incision into the vagina, and the growth is removed as described under abdominal myomectomy in this class of tumors.

TECHNIC IN CERVICAL FIBROIDS.—Occasionally cervical fibroids which grow on the anterior or posterior surface of the cervix may be removed without difficulty through the vagina. The vaginal route should be selected only when the growth is of small size. Growths which develop in the broad ligament are better removed after abdominal incision. If the vagina is not capacious, it may be dilated or enlarged by means of paravaginal incision, after which an anterior or posterior colpotomy is made and the removal

completed under the eye, by the same technic described under abdominal myomectomy. In case there is persistent oozing, it may be necessary to ligate the uterine vessels. The vaginal route is not, at the present time, regarded as the method of choice except for small tumors. Complications may be appreciated better after abdominal exposure.

Abdominal Hysterectomy.—The body of the uterus alone may be removed—supravaginal hysterectomy; or the entire uterus may be extirpated—panhysterectomy. Judging only from theoretical considerations, panhysterectomy is preferable to the supravaginal amputation, since it removes at the same time the chance that cancer may develop subsequently in the cervix. If the woman has borne children, or has a hypertrophied or lacerated cervix, panhysterectomy is the method of choice, if there are no contra-indications. Practically, however, the more complete operation adds somewhat to the mortality in dealing with the larger growths. The operation may be divided further according as the adnexa are or are not removed.

Successive improvements in the technic of hysterectomy have made this operation the most satisfactory method for removing the larger tumors. Its chief objection is that it entails a mutilation of the patient which should be avoided in young women whenever possible. The operation, therefore, should be performed only in the cases in which myomectomy does not seem to be a reasonable procedure. Hysterectomy, therefore, is usually restricted to the larger interstitial growths, to submucous fibroids, to intraligamentous growths which cannot be removed without trauma through the vagina, and to tumors which have undergone some evident degeneration, as well as any tumor in older women which presents indications for operation.

HISTORICAL.—The abdominal hysterectomy for fibroids has been gradually perfected since Kimball, in 1853, performed the first deliberate hysterectomy for an interstitial tumor. Prior to that time, fibroids had occasionally been removed by the more venturesome operators who had opened the abdomen under the impression that they were dealing with ovarian cysts. The earlier hysterectomies carried a tremendous mortality, not only from lack of aseptic technic, but also because of faulty methods of treating the uterine stump after the removal of the tumor. As in ovariectomy, the pedicle was treated extraperitoneally and was transfixed in the abdominal wound because the size of the vessels in the uterine stump made the surgeons hesitate to drop it back into the abdomen. It was usually fastened by transfixion in the abdominal wound with a clamp which was tightened from time to time until the pedicle sloughed away. Subsequently, elastic ligatures and the serrenœud of Cintrat replaced the clamp. There resulted from this treatment a sloughing mass which constantly exposed the patient to dangers of sepsis. Credit for the development of the modern method is due to a group of men, chief of whom are Stimson and Goffe.

Stimson urged that blood vessels should be ligated individually and only after they were isolated. Goffe was largely responsible for covering the cut surface of the pedicle with peritoneum after which the stump was replaced in the abdominal cavity. Subsequent improvements in technic consist largely in the substitution of catgut for the earlier silk ligatures, and proper methods of peritonealization. At the present time, supravaginal hysterectomy carries with it a smaller mortality than the complete removal, in our judgment largely because of faulty technic. Yet, as we have shown, the former method is not always the one of choice. Cervical stumps frequently hypertrophy after the removal of the uterine body, cancer occasionally develops in the stump, and the troublesome leukorrheal discharge may compel a later removal of the cervical mucosa.

GENERAL REMARKS.—The association of sarcoma and fibroids is so common (4 per cent in all cases and 12 per cent in women of more than fifty years of age, according to Sutton) that the specimen should be carefully examined immediately after its removal if the operator does not practice total extirpation of the uterus as a routine procedure. Many advise curetting the uterus as a preliminary diagnostic measure, yet, in our experience, this is not a satisfactory practice. Not only is it impossible often of accomplishment because of a tortuous uterine cavity, but we have frequently observed sarcoma which did not extend into the endometrium.

Both of the methods of hysterectomy are usually done after the vessels have been clamped with hemostats. There is no doubt but that clamps are very necessary in operations in larger tumors, yet a review of a large series of cases will suggest to a critical student that the method may be responsible for many of the emboli which cause a seemingly uncontrollable mortality. It does not seem a reasonable procedure to clamp vessels and ligate them later in an area in which thrombi are already developing. Clamps are always in the way in abdominal exposure and the trauma that is incidental to their handling may quite likely favor extensive thrombi and the subsequent detachment of emboli.

The method of hysterectomy will be described under the headings of supravaginal hysterectomy in uncomplicated cases, panhysterectomy in uncomplicated cases, with or without the removal of the ovaries in each group, as well as the same methods in complicated cases.

TECHNIC FOR SUPRAVAGINAL HYSTERECTOMY IN UNCOMPLICATED CASES.—The technic of this operation varies slightly according as the adnexa are removed or allowed to remain. The subject of conservatism in the removal of ovaries has not yet been settled. There is no doubt but that the removal of ovaries causes ablation symptoms which occasionally are most distressing. Some, as Polak, state that they are more frequent in women in the premenopausal era, yet this does not accord with our experiences as compiled by Maxwell. Ordinarily, ovaries should be allowed to remain in young women when there is no indication of disease; yet even with this qualifica-

tion, we frequently find ovaries which, appearing normal at operation, subsequently develop into cysts which gradually give symptoms.

Preliminary Preparation.—The surgeon should see to it that the patient comes to operation after a thoroughly good night's sleep. It is useless to purge patients preliminary to operation. It is most distressing to learn that a case has been kept awake by griping from a cathartic. We have not purged patients preliminary to operation for more than ten years. Bromids may be given the night before operation to induce sleep. A soap suds enema is given a few hours before operation. The night before operation, the abdomen is washed with soap and water, 70 per cent alcohol, and ether after the pubic area has been shaved. A dry dressing is placed on the abdomen and allowed to remain until the patient is anesthetized. A hypodermic of morphin $\frac{1}{6}$ grain and atropin $\frac{1}{150}$ grain is given a half hour before the anesthesia. The patient is anesthetized with gas and oxygen which is then changed to ether. The vagina is now washed out with soap, water, $\frac{1}{2}$ per cent lysol solution and 70 per cent alcohol. If there is no vaginal work to be done, the vagina is packed with a long strip of gauze, after the patient has been catheterized. The gauze keeps the vaginal walls apart so that they cannot be contaminated by the cervical secretion, elevates the neck of the vagina, and gives a landmark which may be easily recognized in case, after the abdomen is opened, there may be found indications for drainage. Formerly, we prepared the vagina before anesthesia. This is a better procedure in the absence of a trained anesthetist. As a rule, however, it terrifies the patient and makes the anesthesia more difficult. The patient is now placed flat upon the table and the entire surface of the abdomen, the top of the pubic area, and the upper thighs are washed with ether, 70 per cent alcohol, and one-half tincture of iodine. The skin is allowed to dry and the field is made sterile for operation by draping sterile sheets and towels over all save the place selected for incision. The abdomen should never be cleaned with soap and water on the day of operation if iodine sterilization is used.

Opening the Abdomen.—The iodine is now removed with 70 per cent alcohol from the area selected for the incision. This is done so that no iodine may be carried into the abdomen on the gloved hands of the surgeons, or on the pack pads or instruments used during operation. Experience has shown that iodine is responsible for many intra-abdominal adhesions. An incision is made from the pubic hairline to the navel which, in the majority of cases, will suffice for the delivery of the tumor. Occasionally it is necessary to make it somewhat higher and above the umbilicus. It is better to excise the umbilicus in such cases. The incision is made in the midline and is carried through the linea alba. The recti muscles are separated from their sheaths in the midline. The incision should be carried well down toward the symphysis to allow the greatest possible exposure. The last inch in

the lower angle of the wound permits a better exposure of the pelvis than twice that length at the upper end of the incision in the region of the navel. The peritoneum in the upper angle of the wound is picked up carefully and incised between two forceps only after the greatest care has been observed that the intestine is not included in the bite of the forceps. There is always a chance that the bladder is carried up into the abdomen by the fibroid, where it could be readily incised. The peritoneal incision is best made in the very upper angle of the wound. All free sponges should be discarded before the peritoneum is incised, and only sponges mounted on holders should be used while the peritoneum is open. The margins of the incision are now separated with mechanical retractors. The upper abdomen is thoroughly explored and the condition of the kidneys, gall-bladder, stomach, pancreas, spleen, large and small intestine is noted and recorded as a routine procedure. The intestines are now packed off with a large rubber dam and the pelvis is carefully explored. The intestines may be replaced most easily if one starts on the right side of the abdomen, and first packs off the head of the cecum, and then works to the left, placing the pack in such a fashion that the intestines will not come into view during the operation. This method also permits an early inspection of the appendix which, if diseased, may be bound down with adhesions to the tubes or tumor. The larger tumors had better be delivered before the retractors are placed in position or the intestines are packed off. Occasionally these steps of the operation are best not performed until after the tumor has been removed.

Delivery of the Tumor.—The tumor is ordinarily delivered readily with the hand, although a heavy tenaculum or corkscrew is frequently an aid during the procedure. Tumors limited to the body of the uterus can be lifted out readily through the wound, as the unchanged lower segment of the uterus forms a natural pedicle for the tumor. When there are multiple growths, a succession of deliveries may be necessary before the mass can be brought outside the incision. Too great traction should not be made for fear of injuring blood vessels and exciting thrombosis. Sometimes the upper part of the broad ligament must be divided before the tumor can be delivered. Adhesions may complicate the delivery; they rarely give trouble, since they are usually limited to the appendages. Slight, or nonvascular, adhesions not attached to the bowel or other structures which may be injured easily should be broken up with the fingers. Otherwise, they must be treated as their special characters demand. The surgeon should take care in freeing the bowel from the tumor that the line of incision should be made so that there is no chance of injury to the bowel, and that there is a flap of peritoneum left sufficient to cover properly any abraded surface on the peritoneal aspect of that viscus. It is far better to leave a part of the uterus attached to the bowel after the adhesions have been severed than to break through into the intestines, contaminate the field of operation, and create an injury which would demand intestinal resection.

TECHNIC FOR SUPRAVAGINAL HYSTERECTOMY WITH REMOVAL OF THE ADNEXA.—This operation is indicated in women in the menopausal age, irrespective of the condition of the tubes and ovaries. Such a procedure removes all chance of the development of malignant disease in the ovaries at a later period. It should be performed on all women irrespective of their age who present infection of the tubes and ovaries. The removal of the uterus interferes so completely with the circulation of the ovaries that no ovary which is not absolutely normal should be allowed to remain. If it is necessary to remove the tube, the ovary should be taken with it. It is far better to transplant small sections of the ovary into the rectus muscle than to leave any but a normal organ in the peritoneal cavity. Even with these limitations, a considerable number of ovaries will subsequently develop cyst formation.

The tumor is seized with a heavy tenaculum, placed on the side of the uterus, which is to be separated first. The infundibulopelvic ligament is elevated to expose the ovarian vessels which are ligated with catgut. A pedicle needle should be passed through the thin, clear space in the ligaments immediately below the vessel. One should take care that the ureters are not included in their ligatures. It is best to place a second suture distal to the first, and to tie each in three knots so that there is no chance of hemorrhage. The suture should not be placed too high up on the vessels, since they retract after division. The round ligament is next ligated close to the uterus, so that its major portion, together with the adjacent peritoneum, may be left as a flap to peritonealize the raw areas which are made in removing the tumor. The same procedure is now repeated on the opposite side, and two of the four cardinal vessels are thus cut off from the uterine circulation. The uterine end of the infundibulopelvic ligament mesial to the ligation, and the round ligament in the same relative position, are cut through, thus opening the top of the broad ligament and exposing the anastomosing utero-ovarian vessel. The reflux bleeding is controlled with clamps.

Separation of the Bladder and Ligation of the Uterine Vessels.—The uterus is now drawn upward and backward by the tenacula, an incision is made, connecting the opening made by severing the round ligaments at least half an inch above the vesico-uterine reflection of the peritoneum. The fixed portion of the bladder in the midline of the anterior surface of the uterus is cut through with scissors; then the bladder is separated from the uterus with dissecting scissors. This creates less trauma than by stripping the tissues down with a sponge. The cut edge of the broad ligament is elevated and an incision is made between two clamps down to the uterine vessels. The uterus is now brought forward so as to exert traction on the posterior peritoneal covering of the broad ligament in the region of the uterine vessels. This surface is now freed with dissecting scissors and cut through, when the uterine vessels lie exposed. After the bladder is pushed down, the uterine vessels are exposed and ligated with a pedicle or ligature

mounted upon a needle. The same procedure is carried out on the other side. It is quite useless to tie off the blood vessels in the broad ligament as you proceed down to the uterine vessels, since there will be no bleeding of importance after the uterine vessels are ligated in this manner. If the broad ligament is pushed away from the uterus or tumor, and the suture is placed close to the cervix or, in case of doubt, even through its tissues, there is no risk of injuring the ureters.

Incision of the Cervix and Closure of the Stump.—The tumor and the uterus are elevated, while the level of amputation is determined. This site is seized with a tenaculum and steadied while the tumor is removed by cutting through, well above the level of the internal os. The amputation is made by a wedge-shaped incision, to leave anterior and posterior flaps to facilitate a broad, firm closure. It is not necessary to treat the cervix with antiseptics or a cautery in order to sterilize it. Such treatment is more likely to cause complications. The cervix is now closed by uniting the flaps accurately with interrupted or continuous chromic catgut sutures. The sutures should not pierce the cervical canal.

Covering the Abraded Areas.—Any small bleeding points may be included with a suture uniting the vessel to the cervical wall. The round ligaments are brought down and stitched to the posterior margin of the cervical stump with No. 2 chromic catgut sutures. The free edge of the bladder flap of peritoneum is brought back and stitched to the posterior surface of the cervix to cover over the raw edges. The stumps of the ovarian vessels and cut edges of the broad ligament are now closed in the following manner: with a long suture of No. 00 plain catgut mounted on a fine needle, the stump of the right ovarian vessel is inverted just as the stump of an appendix. The knot should be buried and the anterior and posterior flaps of the broad ligament are united so as to leave exposed no raw areas and the minimum of suture material. The suture is continued across the midline of the pelvis, tacking back the bladder flap of the peritoneum to the cervix and proceeding up along the left broad ligament, to finally invert the stump of the left ovarian vessel and leave only a single knot which will be covered by the sigmoid colon. Such a procedure will give an even peritoneal closure, free from raw surfaces or exposed knots which invite adhesions. In case there have been inflammatory adhesions, the peritoneal surfaces should be united so that all raw edges will be extraperitoneal. In case this cannot be done, the sigmoid may be utilized to cut off the pelvis from the abdomen so that the small intestines will not prolapse into the pelvis and become adherent. This method is illustrated in Fig. 49, q.v. All free blood and clots should be removed by the gloved hand of the operator. Unnecessary sponging adds greatly to the peritoneal trauma and favors adhesions. All packs are removed and counted by an assistant who makes certain that their number tallies with that on hand at the beginning of the operation. The peritoneal

cavity should not be closed until the count agrees. No solution whatsoever should be left in the abdominal cavity.

Closure of the Abdominal Incision.—The peritoneum is closed by a continuous plain No. 2 catgut suture, taking care that the raw surfaces are extraperitoneal. As the peritoneum is closed, the omentum should be spread between it and the abdominal wall. The anterior sheath of the rectus and muscle should be splinted by two or three sutures of silkworm gut passed through the skin, fat, fascia and muscle, coming out in reverse order. The closure is completed by uniting the fascia and muscles with double interrupted sutures, taking the greatest care that the upper and lower angles of the wound are firmly approximated. The skin edges are then approximated accurately with Michel clamps, or subcuticular catgut, or a running horsehair suture, and the incision is touched with iodine. Small rubber tubes half an inch in length are threaded on the retaining sutures of silkworm gut so that they may not be tied in a way to damage the underlying tissues by pressure. They should not be tied over a roll of gauze, since, if it is necessary to inspect the wound, the sutures must be cut before there is firm healing. There are many methods in use for the dressing of the wound. The great majority are unnecessary, since most excellent results follow a simple dressing of sterile gauze which is held in place by strips of adhesive.

TECHNIC FOR SUPRAVAGINAL HYSTERECTOMY WHEN THE ADNEXA ARE NORMAL.—Normal adnexa should not be removed in young women. The operation proceeds exactly as in the previous method, save that the incision is made at the margin of the uterus to leave as much as possible of the uterus behind, so that the anastomosing circulation between the ovarian and uterine vessels will be disturbed as little as possible (Fig. 42). Clamps are placed to include the ovarian ligament and tube. The uterine margin of the round ligament is seized with clamps in the same manner. Incision is made between the clamps and the bleeding points are immediately tied with catgut. The ovaries should not remain if it is necessary to remove the tubes, since there is every chance that the ovaries will become diseased from impairment of the circulation. After ligation of the cardinal vessels, all other bleeding points are picked up and tied with the finest catgut that seems practicable. The margin of the uterus which remains attached to the ovarian ligament is sewed to the stump of the cervix and all raw edges are well covered with peritoneum in a manner so that each ovary and tube will lie free and not prolapse in the depths of the pelvis (Fig. 39).

PANHISTERECTOMY IN UNCOMPLICATED CASES.—The complete removal of the entire uterus and tumor is indicated whenever it does not appear likely to add greatly to the risk of the operation. It is indicated in any case in which there is suspicion of malignant degeneration or when the cervix is diseased as a sequence of laceration. The first stages of the operation are identical with those of the supravaginal hysterectomy as far as

the division of the cervix. In the complete operation, it is necessary to separate the bladder below the vaginal insertion of the cervix. After the uterine vessels are ligated, the parametrium should be tied off with another transfixing ligature. Incision of the lower portion of the broad ligament greatly facilitates the elevation of the uterus. The uterus and tumor are

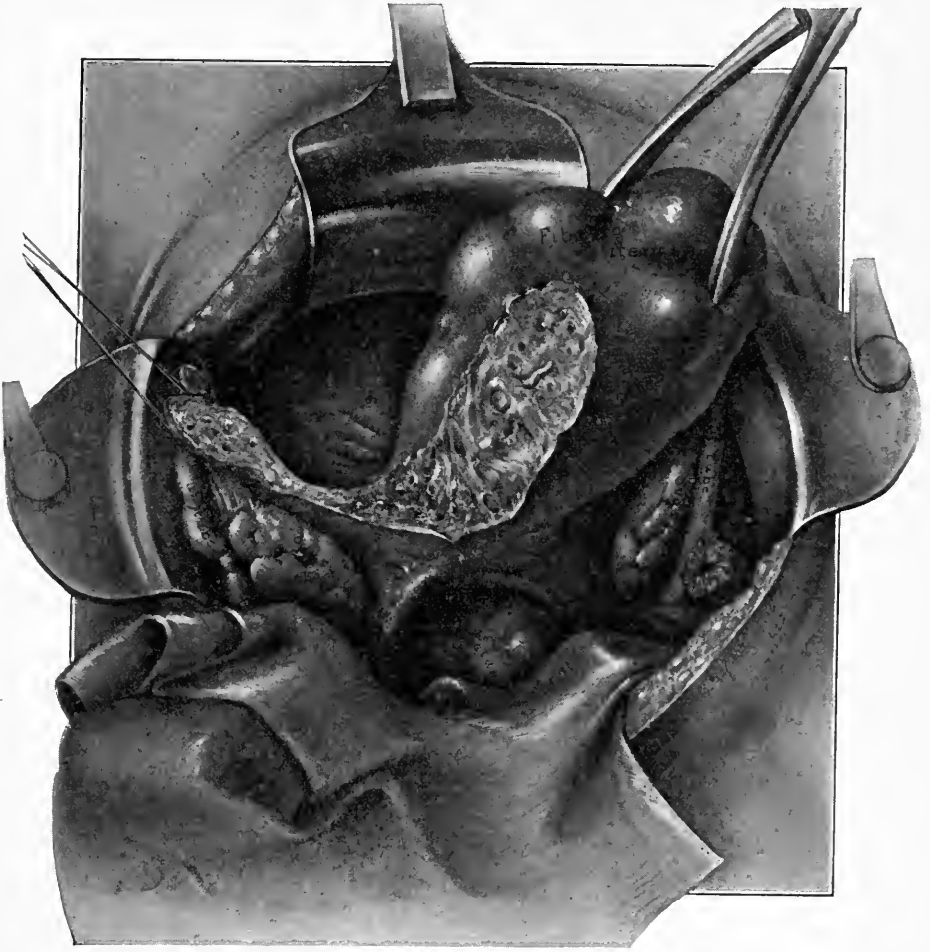


FIG. 42.—HYSTERECTOMY CONSERVING THE TUBES AND OVARIES. Opening the broad ligament. The utero-ovarian anastomosis is preserved in the broad ligament.

now pulled strongly forward and an incision is made on the posterior surface of the uterus just above the insertion of the uterosacral ligament (Fig. 44). By elevating the uterus, the organ may be literally cored from the parametrium. When the organ is liberated, save for the vaginal attachment, the vagina is opened either on the anterior or posterior surface at the cervical margin. The upper vaginal edge is seized with mouse-toothed hemostats and the incision is continued around the upper vagina (Fig. 45).

The hemostats serve as retractors and facilitate closure. There are a few vessels in the parametrium which will bleed and require ligation. They may be clamped and tied, taking the greatest care not to injure nor tie off the ureter which is a very short distance from the incision. The entire

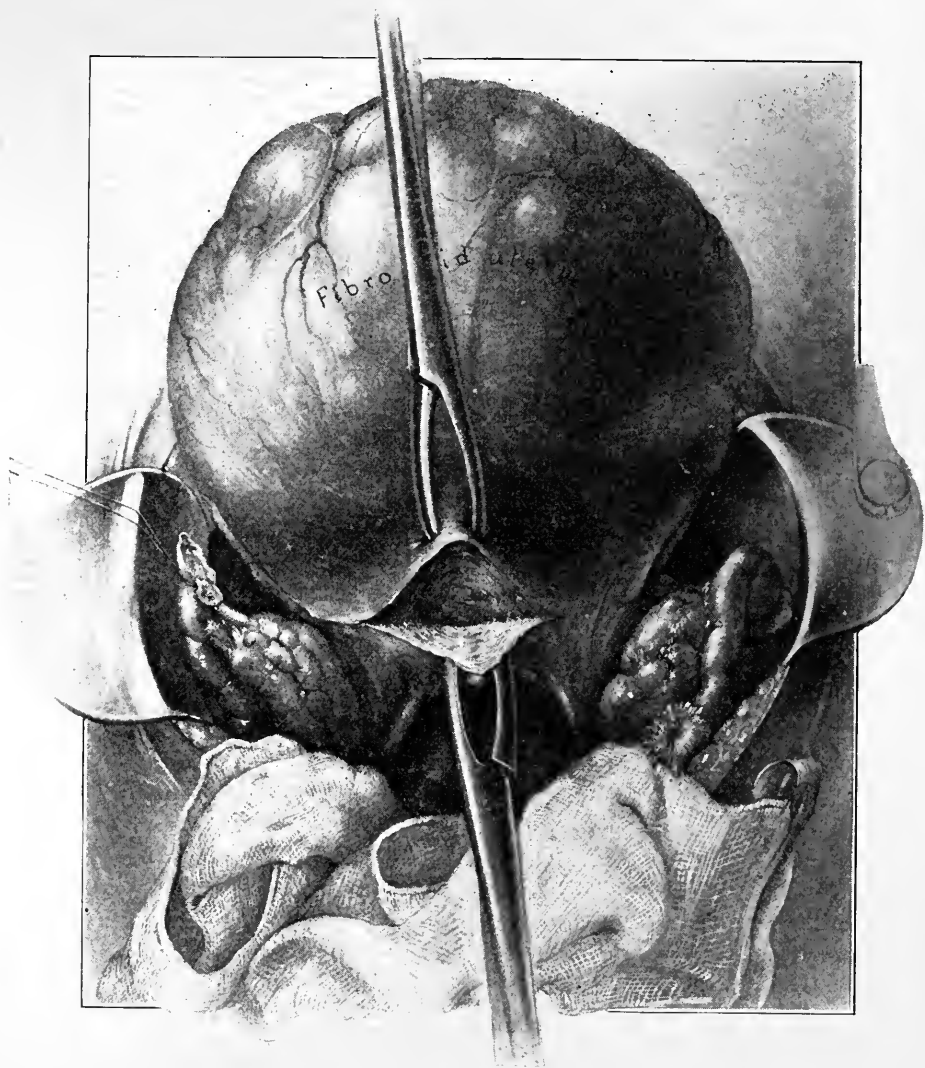


FIG. 43.—SUPRAVAGINAL HYSTERECTOMY. Incision of the cervix.

pelvis should be walled off by gauze packs before incision of the vagina. The vagina is now closed with interrupted chromic catgut sutures. Three sutures should be left as landmarks until the pelvic floor is built up, those on the two sides and the one in the middle. All who have been concerned in the operation now change their gloves, which have been contaminated theoretically by contact with the vagina. All instruments and sutures which

have been used are now discarded. The wound is freshly draped and the packs are removed so that closure may be made under direct inspection. The rubber dam holding back the intestines is not disturbed. The parametrial tissues are united to the edge of the vagina and the fascia of the bladder. The round ligaments are tied to the posterior vagina in the mid-

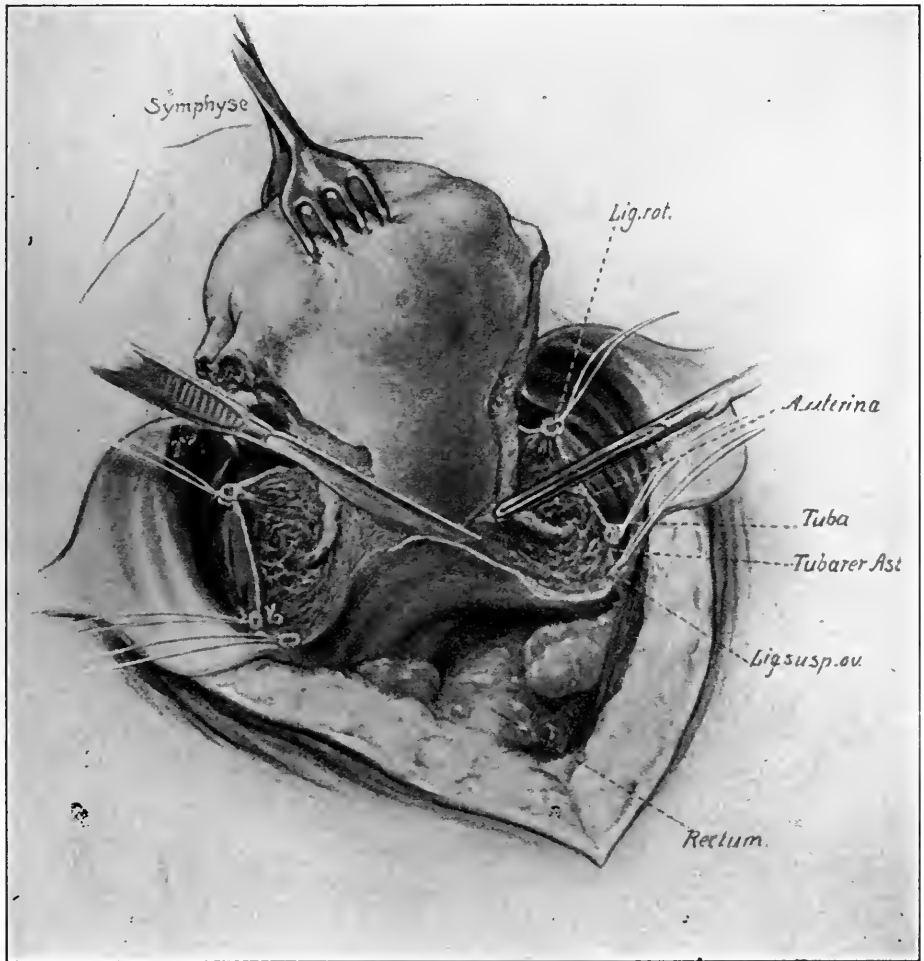


FIG. 44.—PANHYSTERECTOMY. The broad ligaments have been opened, and the posterior peritoneal cuff is being made.

line and near the level of the incision. Peritonealization is made in the same manner described in the previous section (Fig. 48).

ATYPICAL OPERATION IN COMPLICATED CASES.—Serious complications from pelvic infection present so frequently that many operative technics have been developed to meet and overcome them. They all have the same underlying principle of reducing a complicated state to a simple one before

attempting the removal of the tumor. Nearly all these methods attack the adherent masses from below after the removal of the tumor. In our judgment, the average operator will do better first to free the adherent adnexa and to separate such adhesions as bind down the tumor, and then proceed in

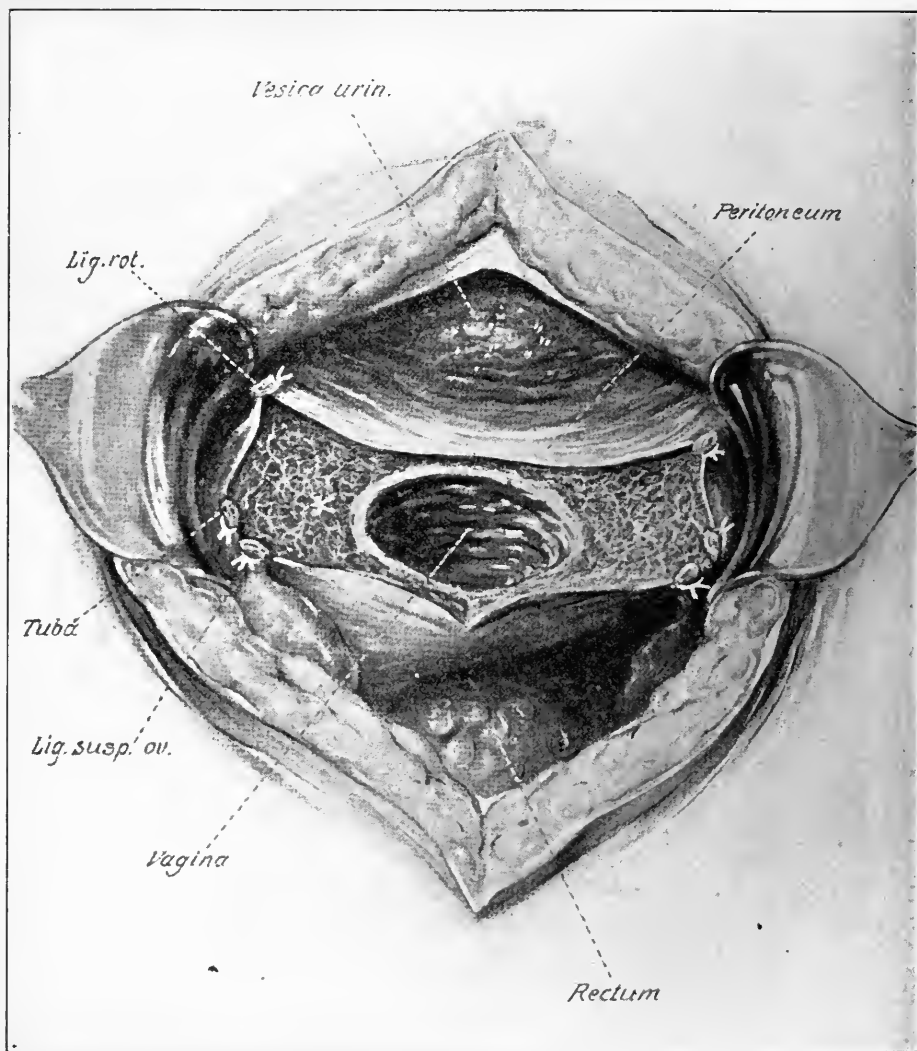


FIG. 45.—ABDOMINAL PANHYSTERECTOMY SHOWING DENUDED AREAS AFTER THE REMOVAL OF UTERUS, TUBES AND OVARIES (Doederlein-Krönig).

a typical manner. If the adherent masses are in the way and landmarks are not visible, the tube and ovary are tied off at the uterine margin and left in place until after the removal of the tumor. The complications will then appear more simple and easier to treat. When the adhesions of bowel are so dense that this does not seem a rational method, exposure may

be obtained by opening the tops of the broad ligaments and obtaining a more safe line of cleavage. If the adhesions cannot be freed from above without considerable chance of serious injury to the intestines, it is better to ligate the ovarian vessels, open up the broad ligament and proceed from below and in front. Occasionally, the capsule of the tumor may be split and the tumor extirpated, leaving the capsule on the intestinal wall for the time being, until the pelvic mass has been removed, when a smooth closure can be made. Cases complicated with abscesses in the cul-de-sac should not be operated until some time after the pus sacs have been drained through the vagina. The risk of infection from the dissemination of pus throughout

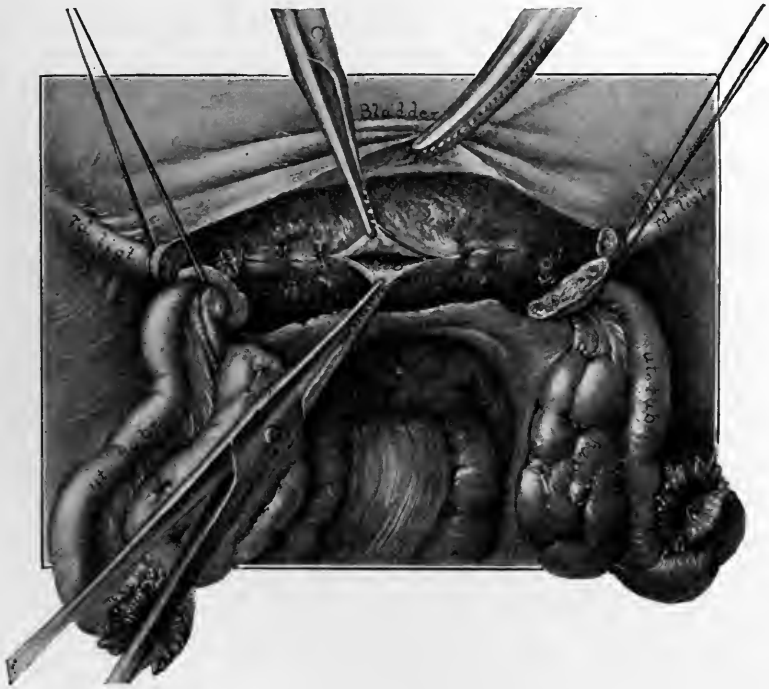


FIG. 46.—CLOSURE OF VAGINA IN PANHYSTERECTOMY.

the wide cellular areas created by the removal of the tumor would constitute a serious menace to the safety of the individual.

The most difficult cases are usually those in which the uterus and tumor are firmly fixed in the pelvis by a pelvic inflammatory condition sufficiently marked as to obscure the important landmarks. The bladder is occasionally forced into a position which further obscures the relationships. The danger from trauma while blindly attempting to break up adhesions is very great, since it may excite serious hemorrhage and scatter infection throughout the entire wound. These cases may be more easily removed after Kelly's method of bisection of the tumor, although there is no doubt that there is considerable danger of infection when operating by this method.

When there is a large intraligamentous growth on one side complicated by adhesions, the methods of Pryor and Kelly will be found advantageous. They are identical in principle, although Kelly's is a supravaginal hysterectomy while Pryor's is essentially a panhysterectomy.

KELLY'S LEFT TO RIGHT OR RIGHT TO LEFT SUPRAVAGINAL HYSTERECTOMY.—This consists in a continuous incision down through one broad ligament across the cervix and up through the other broad ligament, in contrast with the classic method in which incisions are made from above down

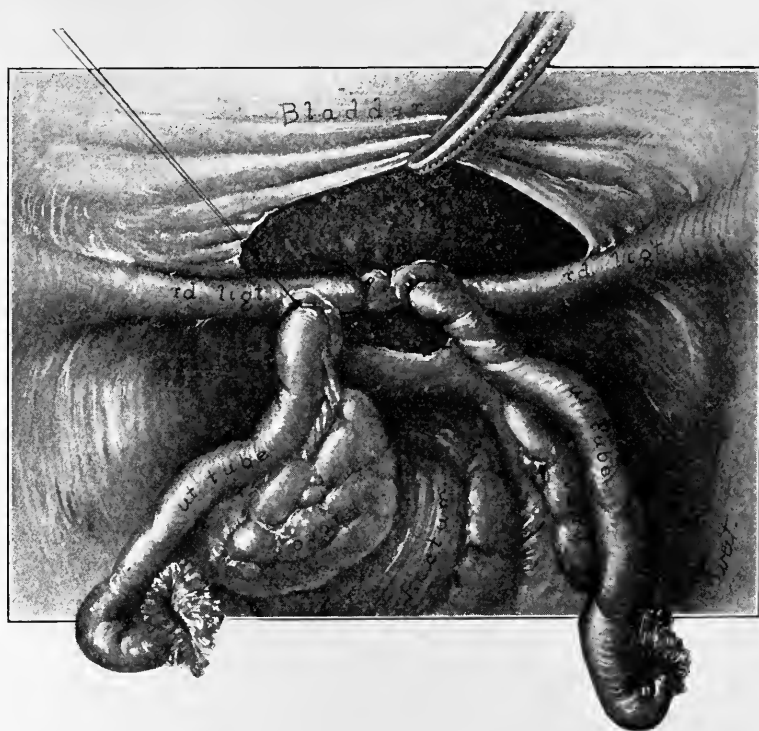


FIG. 47.—PANHYSTERECTOMY. The parametria has been built up in angles of vagina incision. The round ligaments are now sutured to the vaginal vault. The adnexa are fastened near the midline.

on each side of the broad ligament and the vessels are ligated before the cervix is amputated (Fig. 50). It is suited especially to the removal of intraligamentous growths. The start should be made on the side which is more free from complication. The broad ligament on the one side is ligated, as in the more usual operations, and the bladder is separated and pushed down to expose the supravaginal cervix. The edge of the uterus and tumor is now separated from its broad ligament, cutting between clamps until the uterine artery is reached. This is clamped or, in our judgment, better ligated as a primary procedure. The uterine vessels are now divided. A heavy tenaculum is placed on the side of the uterus which has just been

freed, immediately above the level chosen for amputation while traction is made by means of the tenaculum, and the cervix is cut across, coring it to facilitate subsequent closure. When the last fibers of the cervix are severed, the other uterine artery is exposed and caught with forceps half an inch above the level of the cervical level and consequently above the immediate neighborhood of the ureters. By pulling the uterus strongly over to the side which was first freed, the intraligamentous nodule may be shelled out from

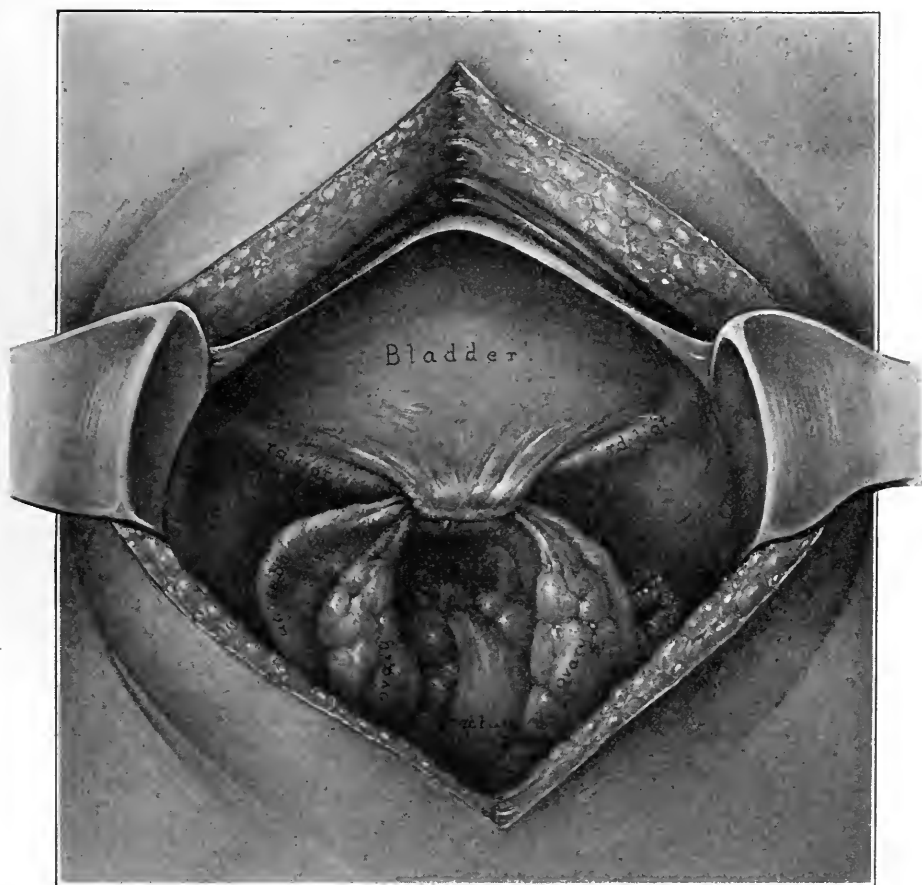


FIG. 48.—PERITONEALIZATION FOLLOWING SUPRAVAGINAL OR PANYSTERECTOMY.

the broad ligament without risk of injuring the ureter. By continued traction, the round ligament and ovarian vessels are now exposed from below, and clamped, or ligated and cut. The incision is now closed in the manner already described.

PRYOR'S METHOD.—Pryor's method of panhysterectomy for tumors of one side is as follows: the ovarian vessels and the round ligaments are ligated on both sides. The bladder is separated and pushed down until the vaginal cervix can be palpated through the anterior vaginal wall. The broad

ligament is incised on the free side from above down until the uterine vessels are exposed and ligated. The uterus and tumor are then held firmly back and up and the vagina is opened in front. The incision is first carried around to the side in which the vessels have been ligated. The uterus is then pulled strongly over to the side presenting the complications; the lateral lower margin of the cervix which has just been freed from the broad liga-

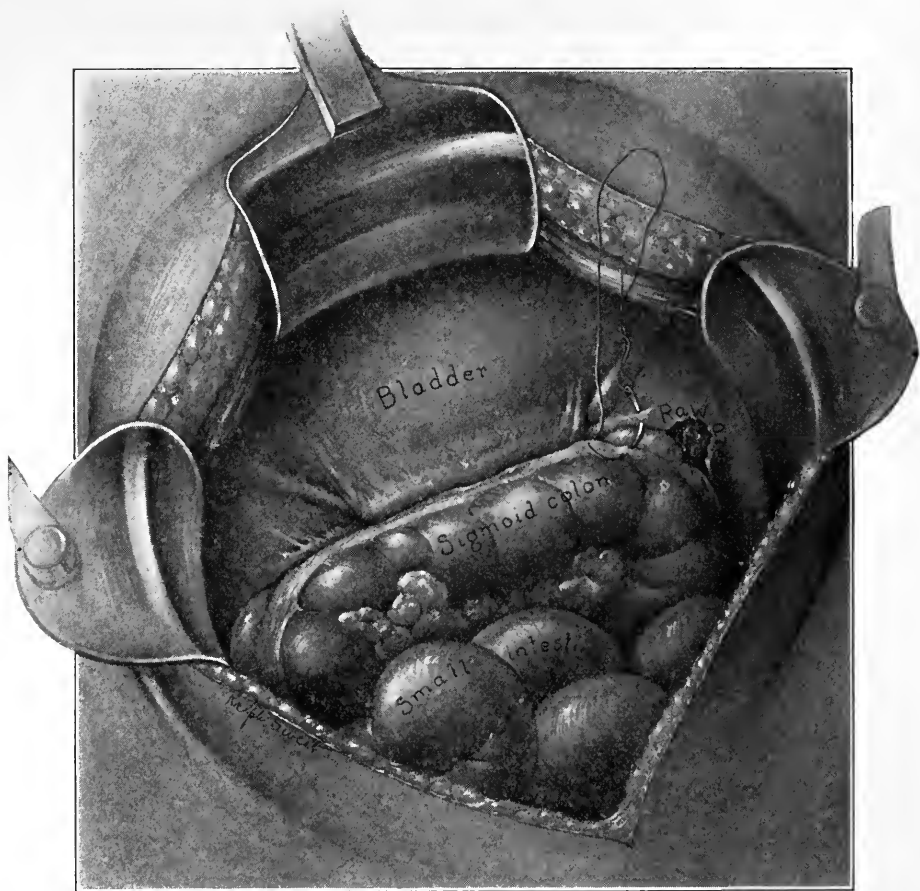


FIG. 49.—PERITONEALIZATION BY THE USE OF THE SIGMOID COLON TO COVER RAW AREAS IN THE PELVIS AFTER HYSTERECTOMY.

ment is seized with tenacula and elevated, thus putting the intact portion of the vagina on the stretch. This is cut through, freeing the cervix and exposing the uterine artery which is ligated and cut very close to the cervix under direct sight. The cut edges of the vagina are clamped together to limit the contamination and covered with gauze packs. The cervix is also covered with a small sponge to prevent extrusion of its contents. The intraligamentous growth can then be shelled out of the broad ligament

without fear of injuring the ureter. The incision is then carried upward as in the previous manner. Although the six cardinal vessels have been ligated, other small vessels may bleed, particularly in the paravaginal tissues. These will require separate ligation. After hemostasis is complete, the vaginal wound is closed in the same manner as described under typical panhysterectomy. This method, while comparatively easy, carries considerable risk of infection, as does any procedure which opens the vagina before the operation is sufficiently developed so that it may be closed immediately.

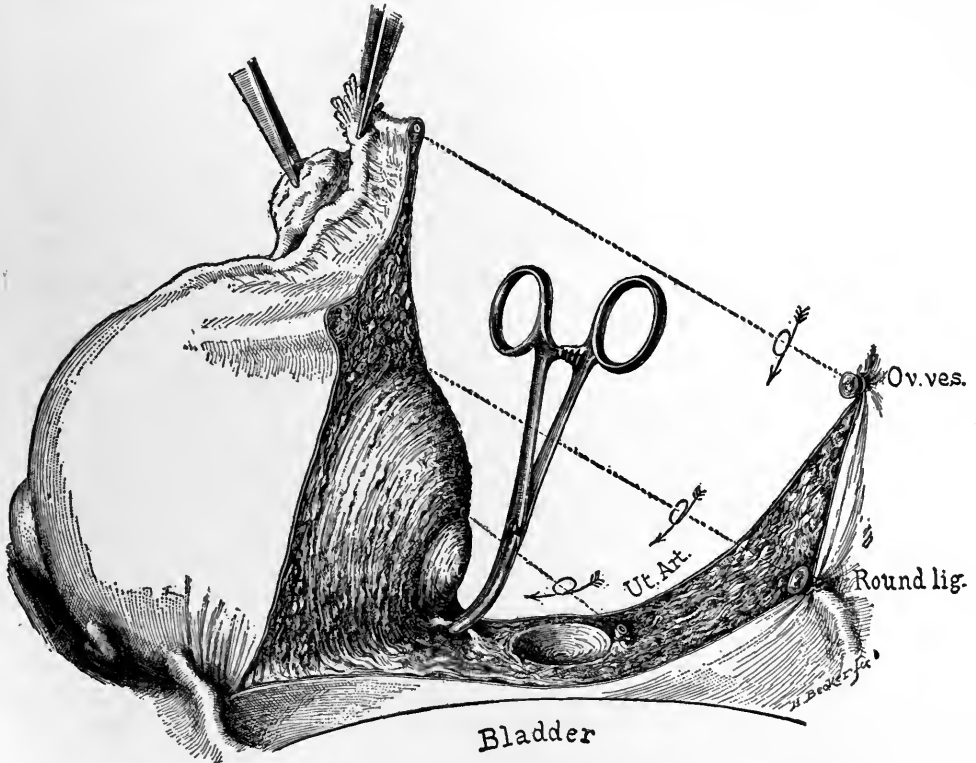


FIG. 50.—KELLY'S LEFT TO RIGHT METHOD OF HYSTERECTOMY (Kelly).

When intraligamentous growths are present in both sides, Pryor advocated a method which first removed the nodules and allowed the ureters to return to their normal position before the uterus was removed. The ovarian vessels and round ligaments are ligated and the bladder is detached from the cervix. The anterior wall of the uterus is elevated with tenacula and is split from the fundus down, through the cervix into the vagina. A lateral incision is then made, through the endometrium through the uterus to the base of the tumor, which is seized and fixed with a corkscrew and enucleated. The posterior wall of the uterus is then divided and that half of the uterus which was first cut laterally is removed. The procedure is then repeated on the other side. This method is not as reasonable as the Kelly bisection method.

KELLY'S BISECTION METHOD.—When the fibroids are incarcerated within the pelvis and held down by a pelvic inflammatory mass, Kelly found that they could be removed very readily after the bisection method. There is, however, considerable mortality attached to this procedure, since one may open very frequently into an accumulation of pus within the uterine cavity. The method is based upon exposure secured by the uterine bisection, thus permitting the growths to be attacked from below the level of their dense adhesions. The bladder is freed from the cervix in the usual manner. Usually, the ovarian vessels cannot be exposed for ligation in the cases in which this procedure is indicated. The fundus is grasped and cut between two large tenacula, directly into the uterine cavity. A large hemostat placed in the cavity will maintain the landmarks. While the incision is made, the uterus is elevated, and the lower portions are raised by seizing them with other tenacula as the incision continues. When the cervix is reached, it is amputated in successive halves, and each half is removed in a manner identical with that described in the left to right or right to left removal. By this means, the enucleation of the inflammatory masses is simple, since the large vessels are easily reached.

There are a number of other atypical procedures which can be used if the conditions appear to warrant them. The best known of these is the *Doyen panhysterectomy* which is so clearly shown by Fig. 43, that further description is not merited. While the illustration depicts the use of this method in a noncomplicated case, it is of greatest value when the tumor is complicated by inflammatory conditions. In such cases, the bladder should be stripped down and the incision made from the front, when the inflammatory masses may be shelled out from the tissues after the vessels have been ligated, as described in Kelly's left to right and right to left method.

Modifications of this method have been described by a number of men. Since they are so manifestly derived from the Doyen method and differ not at all in principle, it is not worth while to attach a name to the procedure. After the uterus has been elevated into the abdominal incision, the posterior portion of the uterus is seized with a tenaculum and the uterus is amputated at the level of the internal os, taking care not to cut into the broad ligament and incise the uterine vessels. While the amputated margin is drawn firmly backward and upward, the broad ligaments are then incised at their edge and the vessels encountered are clamped as they are met with.

TECHNIC IN FIBROIDS DEVELOPING FROM THE POSTERIOR CERVICAL CORPOREAL JUNCTION.—These growths extend downward from their point of origin, burrowing between the rectum and the uterus, carrying the latter up against and above the symphysis and elevating the peritoneum in the Douglas fold. These growths are very difficult to remove without injury to the rectum, since there is no peritoneum between the tumor and the bowel. The safest method of procedure is to separate the tumor at its point of origin, and then remove the uterus by a supravaginal amputation.

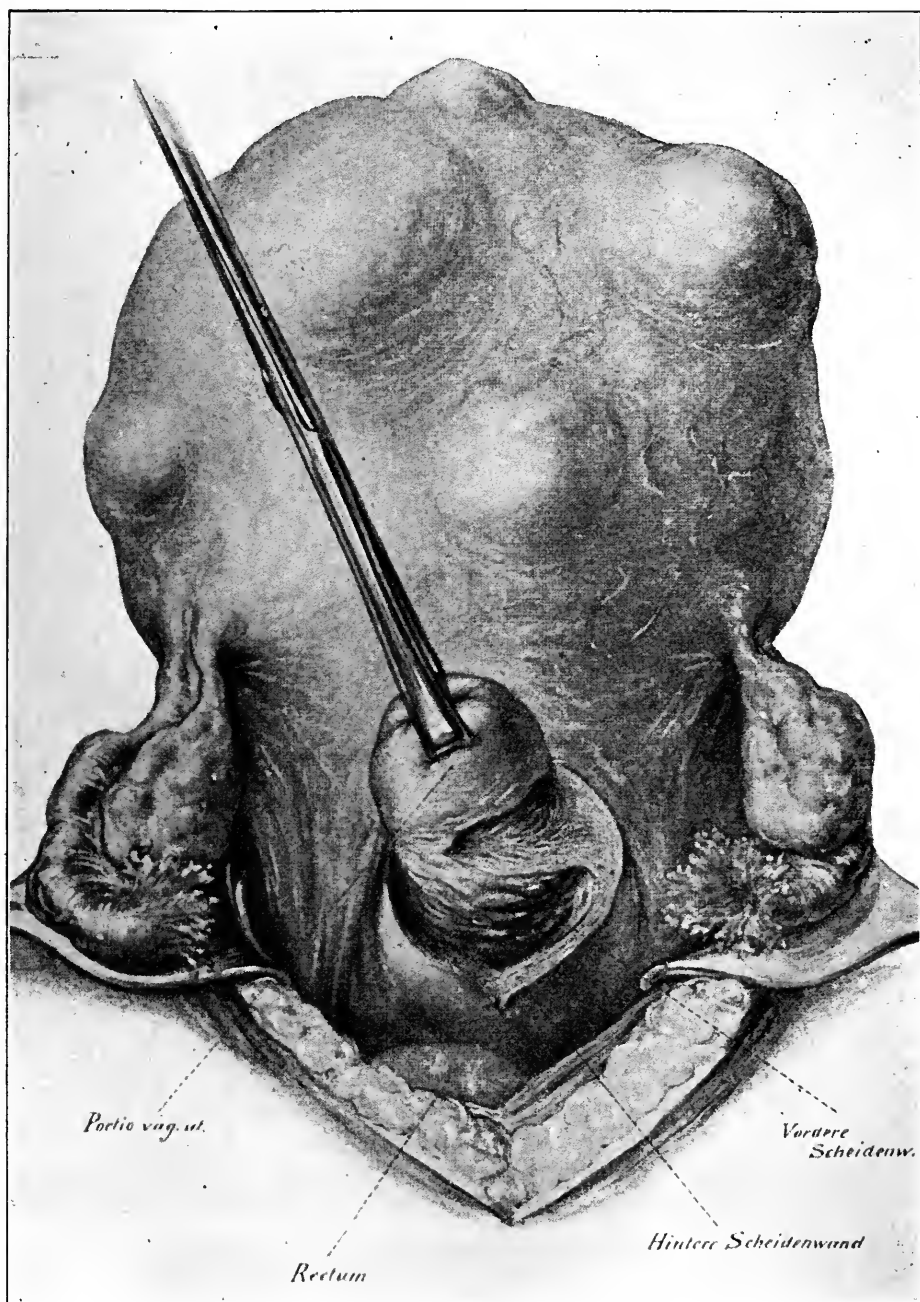


FIG. 51.—DOYEN'S PANHYSTERECTOMY. The vagina has been opened from behind and the cervix seized, elevated and the excision of the uterus begun (Doederlein-Krönig).

The tumor may then be seized on its anterior aspect and the connective tissue capsule split, when the growth may be enucleated, leaving the capsule

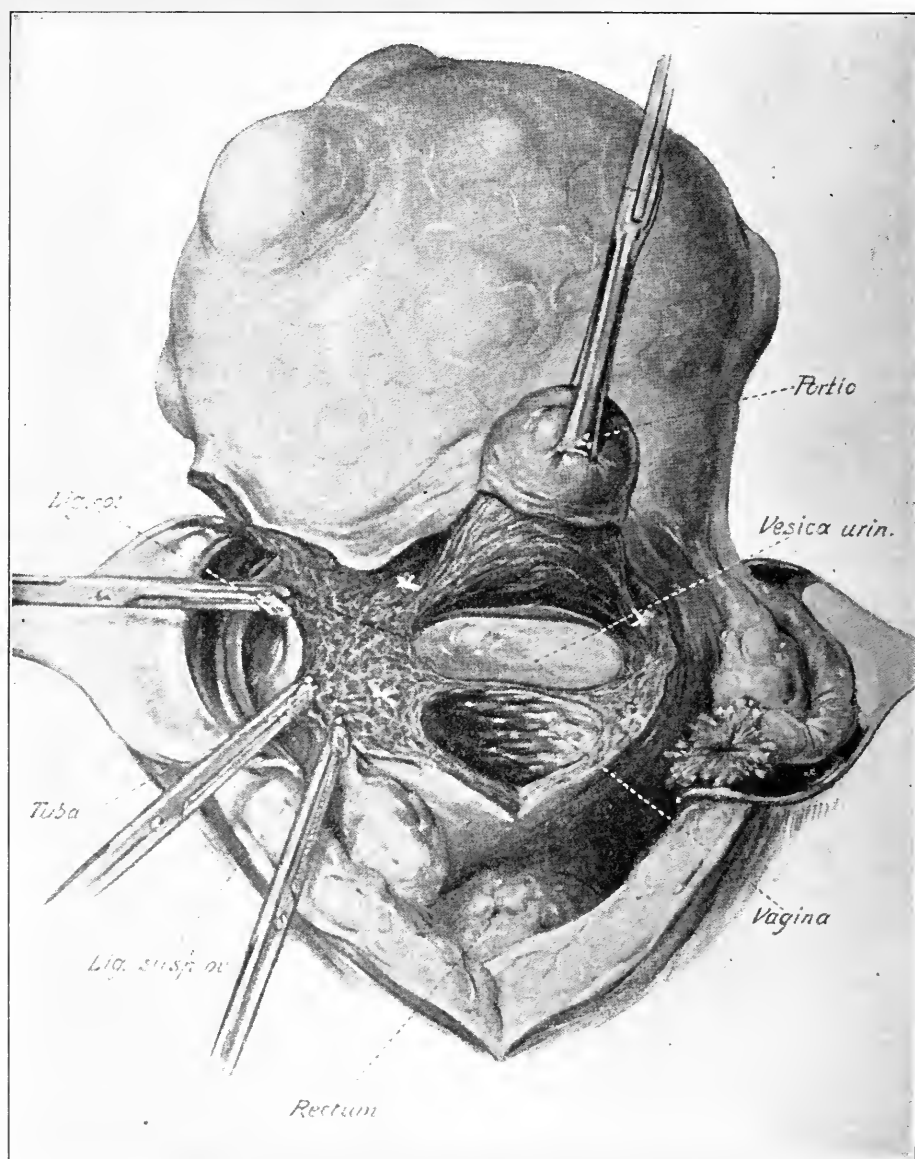


FIG. 52.—DOYEN'S PANHYSTERECTOMY (Doederlein-Krönig).

attached to the anterior wall of the bowel. If hemostasis cannot be made complete, the pocket should be drained through the vagina by a gauze wick.

RELATION BETWEEN FIBROIDS AND PREGNANCY

Sterility.—There is no doubt but that the fibroid statistics of the literature show a higher proportion of sterile marriages than similar cases without known tumors, yet it is an open question whether the fibroids are responsible for the sterility or really result because the man or woman is sterile.

It is very difficult to obtain statistics as to sterility in women in general. In the series of Sims, Simpson, Wells and Duncan, there was sterility in from 8 per cent to 15 per cent of cases. Young and Williams found sterility in 10.5 per cent of 238 women who were medical cases who gave no symptoms referable to the pelvis and who were of the same average age as their series of fibroid cases, that is, thirty-eight and four-tenths years. Hofmeier found sterility in 447 of 2,795 private cases (17 per cent) as contrasted with 441 cases of sterility in 5,462 women in the Polyclinic (8.1 per cent). Goetze found sterility in 7 per cent of 730 gynecologic cases, including those with fibroids. Grünewaldt found sterility in 21 per cent of 900 cases who complained of symptoms referable to the pelvis and in whom congenital conditions were deemed sufficient to account for the sterility in all cases. There is no doubt that the literature shows an increased frequency of sterility in fibroid cases. Olshausen collected the cases of West, Roehrig, Beigel, Schumacher, Scanzoni, Michels, Winckel, Schorler, and Hofmeier and found that 30 per cent of the 1,730 married women who had fibroids were sterile. In the same manner, we have found that sterility existed in 31.5 per cent of 3,617 similar cases, adding to the above series the cases of Schroeder, Young and Williams, Haultain, Goetze, Kelly and Cullen. Yet in our review, we find that errors have crept in from the incorrect translation of some of the earlier series forming the basis of Olshausen's calculations. There are also errors due to the variation in the usage of common terms, since some have accepted as sterile cases which have been pregnant but which aborted before reaching term, while others have included these as fertile. Yet, after making a maximum of deductions, it would appear that approximately 25 per cent of these 3,600 cases were sterile.

Careful review convinces us that tubal and ovarian disease is often responsible for the sterility observed in fibroids. Kelly and Cullen found that both tubes were bound down with adhesions in 364 of their 934 cases; one tube alone was affected in 59 other cases. The ovaries showed some deviation from the normal in more than half the entire series (496 of 934 cases). Young and Williams found inflammatory change in the adnexa of 35 of their 163 cases operated for fibroids. Whether the tumor is the cause of these complications in any marked percentage of cases it is impossible to say. There is no doubt that the

fibroid occasionally may cause adhesions through friction and the reaction attending the various degenerations. Yet venereal infection cannot always be excluded; nor sterility due to the husband. Young and Williams investigated the histories of 31 married women with inflammatory lesions in the appendages. Ten of these were sterile, while 21 had borne children, percentages closely approximating those of the fibroid cases with normal adnexa.

There is no doubt that the location of the tumor has some influence upon the sterility. Schorler, in 253 cases, found sterility in 9 per cent of the cases with fibroid polyps, 16.7 per cent of those with cervical fibroids, 24.7 per cent of cases with interstitial growths, 38.8 per cent of submucous and 47.8 per cent of subserous growths. Young and Williams found sterility in 27 per cent of their cases with interstitial tumors, 31 per cent in submucous cases, and 42 per cent in the subserous (Fig. 44). Goetze arranged his cases in four groups, according to the size and number of tumors and the severity of symptoms. The sterility given for these various groupings ranged from 13.6 per cent for the simple tumors less than the size of an apple, to 50 per cent with growths the size of a man's head or larger. Goetze also emphasized that 91 per cent of his fibroid cases presenting submucous growths had borne children, and calls attention to the rarity with which this form of tumor is seen in nullipara.

Fibroids are more frequent in the fifth decade of life while pregnancy is most common in the third, a difference of twenty years. In attempting to draw conclusions, we should remember that there is ample opportunity during this long period for other conditions to develop which will cause sterility. There are many who believe that in the majority of cases the sterility is the cause of the fibroid rather than the fibroid the cause of the sterility. Nearly all authors unite in stating that "one child," or relative sterility, is commonly observed in fibroid cases. Of 68 cases reported by Pinard, 30 had not been pregnant for more than ten years.

The Effect of Pregnancy on the Tumor.—The tumor increases rapidly in size during pregnancy, according to Caseaux frequently attaining the size of a year's growth in three or four months. Cases are reported where a tumor the size of a hen's egg grew to that of a four-months pregnancy before the end of gestation. The increase in size is partly due to actual growth resulting from the stimulation of the muscle fibers by the increased vascularity and the influence of pregnancy, and partly due to edema. The actual growth is due to the proliferation and hyperplasia of muscle cells, while the fibrous elements do not share so actively in the growth. Occasionally, the growth attains enormous size from edema. Interstitial and submucous tumors are most likely to be affected. Polyps are often reported which, having outgrown the space available in the uterus, are forced into the cervix

without inducing labor. Bleeding may continue during pregnancy with submucous growths. Nauss observed it 19 times in his series.

As the uterus rises out of the pelvis, the tumors attached to it usually become displaced above the pelvic brim. Even growths in the lower segment become drawn up during pregnancy or labor, unless they are on the posterior surface of the uterus and sufficiently large to be impacted in the pelvic cavity. Cervical and intraligamentous growths are not usually displaced, unless they are driven down during labor, sometimes in advance of the head, when they may be forced out

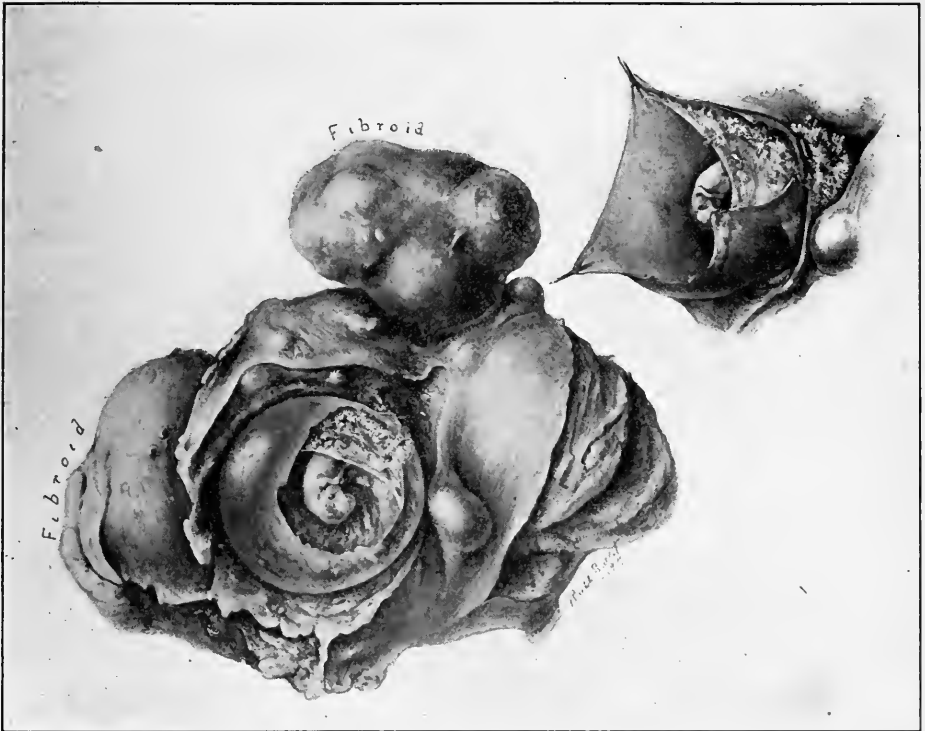


FIG. 53.—PREGNANCY WITH MULTIPLE INTRAMURAL SUBSEROUS FIBROIDS.

of the canal or, more frequently, remain as an obstacle to delivery. As the uterus enlarges and rises up, the fibroids become flattened.

The majority of cases present no symptoms. When symptoms occur, they are usually due to pressure. Cases have been recorded which cause intestinal obstruction. Symptoms occasionally arise from the overdistention of the abdomen and the pressure upon the diaphragm from large tumors late in pregnancy. Various degenerations may occur during pregnancy. Virchow described cyst formation with and without hemorrhage. Tarnier and Mackenrodt emphasized the frequency of necrosis. Torsion of the pedicle may also occur, the twist involving either the tumor proper and sometimes even the womb itself.

Piquand and Lemeland have collected 25 such cases. At a result of the torsion, various degenerations occur, ranging from simple edema to necrosis and gangrene and subsequent peritonitis. Red degeneration is a common complication of fibroids and pregnancy, and is usually responsible for pain occurring in the tumor. It often necessitates operative removal.

Abortion.—Gusserow, compiling the literature prior to 1880, stated that abortion occurs in 21 per cent of cases, but it is not always possible, from his references, to determine whether they were spontaneous or resulted from operative procedures. Chahbazian, in 1882, found spontaneous abortion in 8.2 per cent of his cases. Hofmeier gives 10 per cent. Pozzi, however, in 1909, stated that 5 or 6 per cent more nearly represented the true proportion at the present time. This tendency for the spontaneous termination of pregnancy is also evident in the later months when premature labor occurs. Lefour states that this occurred in 10 per cent of his 227 cases, and Chahbazian in 13.8 per cent of his series. The irritability of the uterus which precipitates labor may be explained by reflex contractions of the myometrium, because of the presence of the tumor, or the frequent association of an unhealthy mucosa or a chronic metritis in fibroid cases. On the other hand, a uterus may be extremely tolerant of both pregnancy and fibroids, and instances of twins and triplets born at term are recorded by Lefour, Carstens, and MacClintock.

Fetal Position.—The position of the child is often changed because of tumors which block the pelvis or encroach upon the uterine cavity. Breech and transverse positions are far more common than under normal conditions. Lynch found that vertex presentations constituted but 59 per cent of 304 cases, breech presentations 22 per cent, and shoulder presentations 18 per cent.

Labor.—Fibroids of the body of the uterus rarely cause dystocia by blocking the outlet. Cervical, intraligamentous growths and pedunculated subperitoneal tumors which have become impacted in the pelvis are far more apt to cause difficulty (Figs. 45, 46). More frequently, they cause uterine inertia by interfering with muscular contractions. The great majority of tumors situated in the lower uterine segment, as well as the smaller cervical growths, may offer no mechanical obstruction to labor, since they are drawn up above the presenting parts of the child during the formation of the lower uterine segment. The cases which are most likely to give trouble are situated on the posterior cervical wall and have become impacted in the pelvis. The important consideration, therefore, so far as the prognosis for delivery is concerned, depends not only on the situation but also on the size of the tumor and its consistency and degree of motility.

The course of labor is frequently delayed due to (a) slow dilatation of the cervix from weak uterine contractions; (b) premature rupture of the

membranes (75 per cent of all cases); (c) faulty presentations (breech and transverse).

There is no doubt but that the second stage may also be prolonged



FIG. 54.—FIBROID IN POSITION TO CAUSE DYSTOCIA.

because of weak contractions. The contractions are frequently very painful. The placenta may be retained and is often difficult to remove manually, particularly if the passage is blocked by growths which have been displaced by the rearrangement of the musculature. Hemorrhage

is a more frequent complication, because faulty contraction and retraction prevent the enlarged sinuses from thrombosing normally. Placenta prævia has been described so frequently that a fibroid uterus must be considered as a strong predisposing factor.

Puerperium.—Danger from complication of fibroids has not been removed with the termination of labor, since many observations suggest that the puerperium may be the most dangerous period.

It is true that many tumors decrease in size during this period, *pari passu* with the involution of the uterus, and give rise to no symptoms. The complete disappearance of a fibroid after labor is not proved. Red degeneration has already been mentioned and may give rise to most acute symptoms in the puerperium. Infection and necrosis of fibroids is particularly apt to occur when submucous growths and interstitial fibroids are forced from their former position into the uterine cavity. We have seen several cases where interstitial growths were expelled from a uterus studded with fibroids during the puerperium (Fig. 53).

Treatment.—It must be remembered that pregnancy associated with fibroids usually runs a perfectly normal course and that obstruction to labor occurs rarely, and usually only when the tumor is situated low down and has become impacted in the pelvis; and that the third stage is frequently complicated by immediate or delayed postpartum hemorrhage. Complications in the puerperium are at least as numerous as they are in labor and pregnancy, and may be of grave significance. No absolute rule can be laid down for treatment, as each individual presents its own problems. In early pregnancies, no treatment is indicated, if there is neither bleeding nor symptoms from pressure. Should pressure symptoms or pain because of degenerations develop, myomectomy is the most conservative treatment in young women, provided, of course, the growth does not encroach upon the mucosa. If the woman is near the menopause, hysterectomy should be done. If the tumor appears to block engagement or obstruct labor in the earliest stages, the patient should be delivered by a cesarean section, after which myomectomy or hysterectomy may be done. There is no doubt, however, that cesarean section is done on myriads of cases with fibroids without proper indication. The degenerative processes which supervene during the puerperium may demand hysterectomy. Hysterectomy is indicated as soon as the growth is known to be infected.

A review of the literature indicates clearly that the great mass of surgeons attending fibroid cases complicated by pregnancy are not conversant with the ordinary course of events. This is shown by a study of Carsten's 516 collected cases. Hysterectomy was done prior to fetal viability in 46.4 per cent of cases. In other words, nearly one half of the cases of the literature up to 1909 were treated as fibroids alone. This treatment was inspired, no doubt, by the fear that the cases could

not progress to term. On the contrary, Lobenstein, who reported in 1911 a series of 100 cases, found that 85 came to term, and that an absolutely spontaneous labor occurred in 75 per cent of his total series,

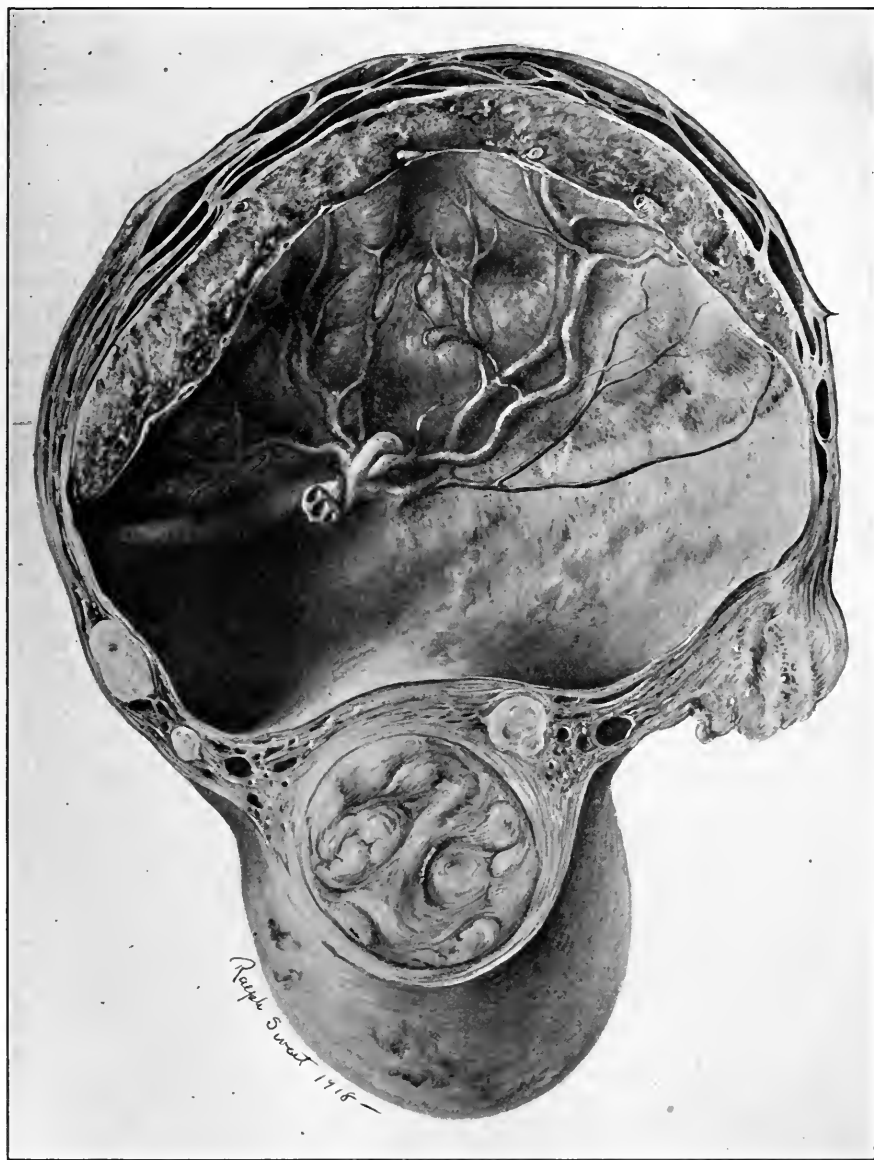


FIG. 55.—INTERIOR OF UTERUS SHOWN IN FIG. 54.

a percentage which was increased to 87 per cent if we include deliveries made with low and mid forceps. Pinard's series, 1895-1901, shows equal results. Intervention was necessary during pregnancy in 4 of

his 85 cases; spontaneous delivery ensued in 54 cases. Spontaneous delivery ensued in 64 per cent of Pinard's series of 1901-1904, and in 68 per cent of Troell's series. With statistics like these in the literature, there is no doubt that definite and compelling indications are necessary to justify operations during pregnancy.

Myomectomy appears to us as a surgical curiosity, with rather a narrow field for the treatment of fibroids complicating pregnancy, because it is most difficult to perform successfully in the class of cases in which interference is most frequently demanded (pelvic impaction); as well as the fact that subsequent adhesions are almost the rule; and there is the ever present possibility that the scar may rupture during labor in the event that the case escapes abortion and comes to term. Yet, in spite of all theoretical objections, the operation has enjoyed wide vogue. Tumors of fifteen, sixteen, and seventeen pounds have been removed successfully (Netzel, Schorenz, and Edgar). Abortion has been reported in less than one-fourth of the cases; thus, Turner reported that 17½ per cent aborted in 44 myomectomies (1890-1900); Thumin, 28.4 per cent aborted in 102 cases (1885-1900); Le Maire, 26.4 per cent aborted in 93 cases (1892-1901); Carstens, 29.1 per cent aborted in 150 cases up to 1909; Troell, 23.9 per cent, in 157 cases (1900-1909). A review of these figures indicates that cases should be carefully selected for myomectomy and that none should be operated without compelling indications.

CHAPTER VII

ADENOMYOMA OF THE UTERUS AND OTHER PELVIC STRUCTURES

Definition—Frequency—Etiology—Wolffian theory—Müllerian theory—Adenomyoma of the uterus—Cullen's classification—Appearance of growth—Microscopically—Subperitoneal and intraligamentous adenomyoma—Submucous adenomyoma—Cervical adenomyoma—Degenerations of uterine adenomyoma—Cyst formation—Carcinoma—Sarcoma—Tuberculosis—Condition of tubes and ovaries in adenomyoma—Symptoms of uterine adenomyoma—Physical findings—Diagnosis—Prognosis—Treatment—Other forms of adenomyoma—Adenomyoma of the rectovaginal septum—Symptoms—Physical signs—Treatment.

Adenomyoma forms a distinct class of fibroids. It is composed of glandular elements imbedded in fibromyomatous tissues. Occasionally, the growth is diagnosed prior to operation because of distinctive symptomatology and clinical findings. Adenomyoma may be found in any part of the uterus, the tubes, ovaries, round ligament or rectovaginal septum. While the female pelvic organs contain most of these tumors, they have been observed in other parts of the body, bowel, stomach, gall-bladder, kidneys, etc.

Frequency.—The fact that fibroids could contain glandular tissue has been known for many years. As early as 1884, Schroeder, Herr and Grosskopf collected 100 such cases. Yet these tumors were not recognized universally as a distinct type until von Recklinghausen, in 1896, focused attention upon them, since when they have been the subject of much investigation.

There are comparatively few reports which indicate the frequency of the disease. The great majority of the tumors have been discovered accidentally in the laboratory in the routine examination of fibroids after their removal. The only comprehensive report is given by Cullen, who, in 1908, reported that 5.7 per cent of 1,283 fibroids which came under his observation were proved to be adenomyomata. It may be possible that this percentage is lower than the actual occurrence, since the presence of adenomyoma can be excluded only when the entire fibroid has been cut into thin cross sections, and subjected to microscopic study. Because of the enormous labor entailed by such a procedure, only the more suspicious cases were so treated in Cullen's laboratory.

Etiology.—The etiology is unknown, although usually ascribed to congenital causes.

In the absence of definite etiology, investigators have confined their studies to the origin of the epithelium. The majority believe that the tumor is a true adenoma, and is composed essentially of epithelium, and that the muscular elements are secondary. Others believe that it differs from an ordinary fibroid only in that there is a secondary extension of glandular tissue from the endometrium into the fibroid mass. Von Recklinghausen recognized two types of tumors classed according to the origin of the epithelium. He based his opinion on the examination of 34 uterine and tubal adenomyomata. In one he considered that the epithelial elements were derived from portions of the original wolffian bodies which were pinched off in early fetal life and after remaining long dormant developed into the glandular structures. This type, he believed, was situated in the periphery of the uterus and in the tube. In the other type, the glandular elements arose from the uterine mucosa. He considered that the latter cases were rare, since he could demonstrate a connection between the uterine mucosa and the glandular spaces of the tumor in but a single instance. He studied 23 uterine tumors. In the great majority of the larger growths, he found a characteristic arrangement of the glandular tissue. There was one main canal, into one side of which ran many subsidiary tubules which radiated outward like the sticks of a fan. The tubules were close together like those of a kidney. There were also numerous cystic dilatations in the secondary tubules which, since they were situated in the periphery, presented as a medullary zone. The whole picture suggested the possibility that the epithelial elements originated from the wolffian bodies, a view which was strengthened by the fact that nearly all such cases were found near the tube and on the posterior surface of the uterine wall; in other words, near the site of the wolffian bodies. Von Recklinghausen's theory was presently adopted by Pick, Breus, Voigt, Pfannenstiel, Krönig, and others.

In marked contrast to this theory is Cullen's view that the epithelial elements are derived from the glands of the endometrium. This observer, in 1903, presented a monograph based upon the study of 22 cases, all of which were studied by serial sections. In nearly all the cases, the glands of the tumor were found to be continuous with those of the endometrium. The epithelium of the tumor resembled that of the uterine glands and often presented areas of blood which suggested that these detached islets of uterine mucosa carried on the menstrual function. In 1908, Cullen presented an extensive monograph based upon a study of 56 cases of diffuse adenomyomata of the uterus. The continuity of epithelium between endometrium and tumor was demonstrated by serial sections in 55 of the 56 cases. Cullen's hypothesis appeared strengthened by the case reported by Whitridge Williams in which the uterus of a woman dying shortly after labor contained decidual areas in the glands of a diffuse adenomyoma. Similar findings

in an adenomyoma complicated by tubal pregnancy were observed by Cullen.

The predisposing causes for adenomyoma are not known. The majority are inclined to the belief that the condition is favored by a preëxisting chronic inflammation of the endometrium. Chiari, von Franqué, Leguen, Marien, and others, have advocated this theory, at least in part. Others lay stress only on mechanical factors and consider that the opportunity for mucosal invasion is brought about chiefly by gestation and labor.

Some see, in the extension of the uterine mucosa into the fibroid tissue, an example of epithelial heterotopy, a term applied by Robert Meyer to characterize a nonmalignant invasion by an epithelial membrane. They associate this process with the result of inflammation and regard it as a healing process after cell injury and degeneration.

Iwanoff, in 1898, advocated the view that the glandular structures were derived from the serosa by metaplasia. He also saw an inflammatory process as a predisposing condition, under which stimulant the peritoneal epithelium proliferates and sends down buds of cells into the subadjacent tissues. These then proliferate and form branching tubular adenomatous processes. He states that the metaplasia of cells is so complete that the crypts are lined by columnar epithelium, and that the appearance is indistinguishable from one derived from the invasion of a true mucous membrane. He also argued that the connective tissue adjacent to the adenomatous processes changes in character as a result of inflammation and becomes the cytogenous tissue which is one of the chief features of the adenomatous growth. He adduces sections showing the change to support his view. Sitzenfrey, and others, have presented similar findings. At the present time, it does not seem as if all the cases of adenomyoma could be explained by one theory. There is no doubt, however, but that the comprehensive studies of Cullen prove that nearly all cases, at least of diffuse adenomyomatous growths of the uterus, are derived from aberrant uterine tissues.

ADENOMYOMA OF THE UTERUS

The following classification is given by Cullen: (1) adenomyoma in a uterus of relatively normal contour; (2) subperitoneal and intraligamentous forms; and (3) submucous growths.

Adenomyoma in a Uterus of Relatively Normal Contour.—The uterus is rarely enlarged in these cases to more than three times its normal size. Adhesions are usually present and may be so dense that the removal of the uterus is often attended with much difficulty. The size of the tumor varies, although it may be so extensive as to involve one side of the uterine wall. The posterior wall is more commonly

involved, although the tumor may be present on the anterior side. When the growth is developed almost entirely in one wall, that side of the organ is unusually thick. On section of the uterus, the diagnosis may be made macroscopically. The characteristic features are a uniform increase in density without evidence of a circumscribed tumor and the presence of the adenomatous processes which are visible to the

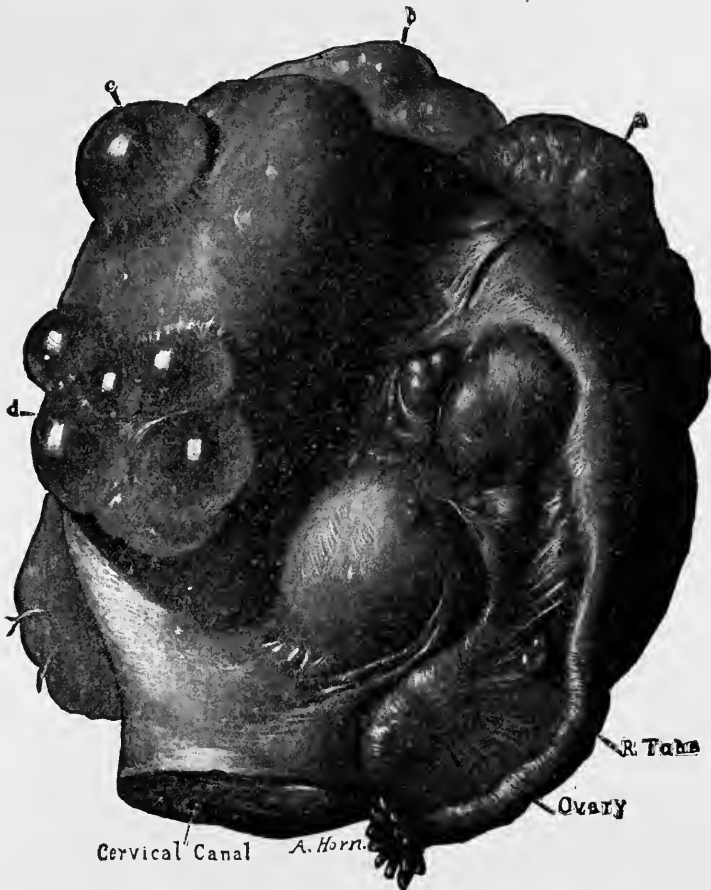


FIG. 56.—CYSTIC ADENOMYOMA WITH NUMEROUS NODULES AND SUBPERITONEAL CYSTS (Kelly).

naked eye. The endometrium is usually normal, but may be hypertrophied or occasionally attenuated. The adenomatous growth extends to, but not into, the endometrium. The other muscular coats are usually normal. The tumor itself is of variable thickness and appears as a mass of coarsely fibrillated fibers arranged in whorls, in which there are scattered areas of a homogeneous translucent tissue resembling mucous membrane. Cystic spaces are occasionally found in these areas, although they are seldom of considerable size. The

glandular areas frequently present a brownish discoloration which in the cystic zone may be seen to be due to a chocolate-colored fluid. Small fibroids may be present in other parts of the uterine wall. They stand out as pale and more definitely circumscribed and offer a strong contrast to the diffuse, pinkish, hyperplastic areas which are found in the adenomyoma.

Microscopically, the growth is seen to be composed of fibromyomatous tissue in which are imbedded glandular structures. The former differs from that usually found in fibroids only in that there is no definite encapsulation, since the tissue merges gradually into the surrounding muscular wall. The glandular tissues present as irregular masses of varying size and shape which may be scattered throughout the tumor but usually are more abundant near the uterine cavity. The glands suggest those of the normal endometrium, although their outline is more irregular. They are of tubular form, and frequently open into one chief canal which later may become a cyst of some size. The glands are imbedded in cellular tissue as in the normal endometrium. The arrangement of the glandular tubules is not uniform. Occasionally, they enter the terminal canal only on one side, presenting an outline similar to that seen in the ducts of the glomeruli of the mesonephron. This picture strongly suggests tissues of the wolffian body. Yet Cullen demonstrated their continuity with the endometrium in practically every case. The ducts are lined with a single layer of ciliated columnar epithelium, containing an oval vesicular nucleus in the base of each cell. The stroma also resembles the endometrium and contains thin-walled blood vessels. The cyst spaces of the central duct contain old blood and pigmented cells which Cullen believes are the result of menstrual changes.

Subperitoneal and Intraligamentous Adenomyoma.—These forms develop by processes identical to those noted in the production of similar types in ordinary fibroids. A tumor which develops above the middle of the uterus, and grows outward underneath the peritoneal investment of the uterus, constitutes a subperitoneal tumor. In contrast, a growth which originates below this point and grows to the lateral side of the uterus is likely to develop between the folds of the broad ligament, when it is termed intraligamentous.

Subperitoneal adenomyoma may vary in size and shape. They are usually sessile and rarely present with a definite pedicle. Cullen found 8 subperitoneal growths in his 56 tumors. In contrast with diffuse types of adenomyoma in a uterus of normal outline, the subperitoneal adenomyomata are usually cystic. The cysts vary in size from microscopic areas to masses which practically fill the tumor. They are usually multiple and contain chocolate-colored fluid. They present different colors, depending on the amount of myomatous tissue which they contain. As a rule, they are dark colored. Occasionally, the

cystic growth can be seen shining through the peritoneal coat of the uterus. There is no doubt but that many of these cases are mistaken for peritoneal inclusion cysts. The masses are usually but not uniformly covered by adhesions. The cyst walls are composed of fibromyomatous tissue lined with a well-defined membrane, whose epithelial elements are cylindrical, ciliated epithelium in a single layer.

The intraligamentous forms are similar to the subperitoneal variety, although the cysts may attain extremely large size. Breus described one which contained seven liters of fluid. Lockyer believes that many of these growths may arise from the wolffian system, and possibly Meyer's theory may explain others, although Cullen's microscopic pictures cannot be regarded lightly.

Submucous Adenomyoma.—These are the rarest forms of uterine adenomyoma and differ from those previously described in that they present as polyps. The structure of this form is identical with that of the diffuse type. Cullen believes that they develop as a diffuse growth and become polypoid as a result of uterine contraction which finally forces them from their bed just as the ordinary fibroids may be excluded from the uterus. Cyst formation is rare, possibly because of the pressure exerted by the uterus on all sides of the tumor. The mucosal covering varies, just as it does in the ordinary fibromyomatous polyps.

Cervical Adenomyoma.—This type is occasionally encountered. It presents in various forms, depending upon the direction of the tumor's growth. Rarely it grows into the cervical canal and attains considerable size. Landau and Pick have described a case in which the cervical canal was entirely obliterated by the tumor. The histologic picture is similar to that of the preceding forms, save that the glandular areas resemble cervical glands. Sometimes growths which develop from beneath the uterine endometrium extend downward below the internal os. They should not be confused with adenomyoma of the cervix.

Degenerations of Uterine Adenomyoma.—Degenerations, with the exception of cyst formation, are very unusual in this class of tumors. This is undoubtedly due to the good circulation of the growth. As has been noted above, the cysts are due to the deposit of menstrual fluid in the pockets of the growth. Their ultimate size is dependent upon the resistance offered by the uterine wall and the pressure that is exerted by the menstrual secretion.

Carcinoma is a rare degeneration of the adenomatous tissue. It may originate in the epithelial elements of the tumor or may extend into the mass as a secondary invasion from a carcinoma which has been primary in the uterus. Primary carcinomatous degeneration has been recorded by Rolly, Babescu, Schwab, Dillman (2 cases), von Recklinghausen (3 cases), while combined cancer of the uterus and adenomyoma have been described by a number of men. Cullen cites 6 cases of epithelioma of the cervix, together with diffuse adenomyoma of the body of the uterus. Also 2 cases

of diffuse adenomyoma in conjunction with adenocarcinoma of the body. Grünbaum describes a case of cancer of the body and adenomyoma of the cornua.

Sarcoma is infrequently associated with adenomyoma. Iwanoff, Bauereisen, and Kaufmann each have described cases.

Tuberculosis is more commonly observed as a complication. In fact, tuberculous lesions have been so frequently found in salpingitis isthmica nodosa that many authors have come to regard the tubercle bacillus as an etiologic factor in adenomyoma. This is not, however, substantiated by Meyer. Tuberculous degeneration of adenomyoma has been recorded by von Recklinghausen, Lichtenstein, Hoelsi, Archambault, Pierce, and Landau, while Lockyer and others have noted the association of adenomyoma and tuberculosis of the fallopian tubes.

Condition of the Tubes and Ovaries in Adenomyoma.—Cullen described the condition of the tubes and ovaries in 45 cases. They were normal, in 15 cases. Numerous adhesions were present in 30, due, he believed, to a mild degree of pelvic peritonitis caused by the diffuse adenomyomatous growth. Inflammatory changes were noted in one half of Landau's cases. Polano and Kudoh found adhesions in 89.5 per cent of cases (72 cases in the series). Cullen found adhesions on the uterus in 24 of 49 cases. They were usually only on the posterior surface. The literature indicates that adenomyoma is far more frequently associated with pelvic peritonitis than is the ordinary fibroid.

Symptoms of Uterine Adenomyoma.—The symptoms vary according to the size and location of the growth and the condition of the adnexa. The symptoms are usually hemorrhage and pain.

Hemorrhage is common and usually presents, at first, as a prolonged menstrual period. With the development of the tumor, the bleeding may be so great as to occasion alarm. The hemorrhage is readily explained when we take into consideration the greatly increased area of uterine mucosa, so that both the endometrium of the uterine cavity and the patches scattered throughout the tumor share in the process.

The *pain* may be a dull ache, or it may be grinding in character. In the cases first presenting symptoms, the pain is generally limited to the uterus but may be referred to the back and legs. It is thought that the pain results from nature's effort to expel the tumor as a foreign body at a time when it is engorged with blood.

Leukorrhea is not ordinarily seen in cases presenting only adenomyoma. If there are old foci of infection, it may be present, but not necessarily as a result of the growth. Intermenstrual discharge is very rare.

Physical Findings.—The physical findings are, as a rule, not distinctive of adenomyoma, but are those of the ordinary fibromyoma complicated by pelvic inflammatory disease. The type of tumor that preserves the normal outline of the uterus may present only an enlarged uterus. Since dense adhesions are not the rule in these cases,

the uterus may be freely movable. Lockyer emphasizes the fact that ordinary fibroids are usually present in association with these tumors. The intraligamentous forms are more firmly fixed in the pelvis than are the ordinary fibroids. Occasionally, they may simulate a pelvic abscess. Tumors of the rectovaginal septum may readily be confused with pelvic inflammatory diseases or with rectal carcinoma.



FIG. 57.—ADENOMYOMA OF POSTERIOR UTERINE WALL.

Diagnosis.—Generally speaking, the case is regarded as an ordinary fibroid until it has been cut open in the operating room. Occasionally, however, cases present certain features which are, at least, strongly suspicious of this condition. Freund, in 1896, stated that these tumors presented a definite clinical picture by which they could be diagnosed. Cullen agrees with this view and states that while he failed to detect it clinically in the early stages of his investigation, he is now convinced that diffuse adenomyoma of the uterus presents symptoms so suggestive that hospital assistants may at least suspect the condition. He emphasizes that when a physical examination has disclosed an enlarged adherent uterus, the following clinical facts point strongly to adeno-

myoma: (1) the bleeding is usually confined to the menstrual period; (2) there is commonly much pain during menstruation referred to the uterus; (3) there is usually no intermenstrual discharge of any kind; and (4) the uterine mucosa is perfectly normal and is rather thick, although this finding can be observed only after curettage.

Freund urged that patients presenting uterine adenomyoma usually presented a history of (*a*) a sickly childhood; (*b*) delayed onset of menstruation; (*c*) profuse and painful periods; (*d*) irregular hemorrhages, pelvic peritonitis and marked anemia; (*e*) bodily functions impaired so that ordinary activities are more or less impossible.

These views are not supported by the majority of other observers. Grünbaum combated it from study of a series of 20 cases in Landau's cases. Polano and Kudoh obtained no corroboration from a study of 100 cases. The average age of Landau's cases was forty-one years. Forty-five per cent of Polano's 66 operative cases were in the fifth decade. Volk recorded a case in a virgin, aged twenty-five years. Treub operated cases of sixty-nine and eighty-five years. Polano found that menstruation was established between twelve and nineteen years, that it was regular in 63 per cent and irregular in 37 per cent. It was excessive in 62 per cent, normal in amount in 18 per cent, and scanty in 18 per cent. Only 9 of Grünbaum's 20 cases complained of severe pelvic pain during menstruation. Ten of Grünbaum's cases were very well developed and infantilism was rare. Only one instance gave a history of delayed onset of menstruation. In our experience, uterine fibroids are often associated with pelvic inflammatory disease. This group of cases is many times more frequent than that of the adenomyoma, and the symptoms are practically identical. In consequence, we very often suspect adenomyoma and find at the operation that the condition is only a fibroid complicated with inflammation. We believe, therefore, that an opinion expressed before operation amounts only to a possibility.

Prognosis.—The prognosis without operation is undoubtedly worse than in ordinary fibroids, because the growth which causes hemorrhage and pain is usually complicated by pelvic inflammatory processes. There is no doubt but that curetting and medical treatment aggravates the conditions. The danger in neglected cases is from hemorrhage, which in at least one case, that of Fritz Volk, led to death. Because adenomyoma is better nourished than the ordinary fibroid, it is not liable to degenerative changes. There are no records of sloughing or gangrenous adenomyoma, although cystic formation may occur to an extreme degree. While adenomyoma may predispose to carcinoma, this degeneration is not very frequent. The intimate relationship with pelvic peritonitis is of great importance from the viewpoint of prognosis. The association of inflammations of the adnexa, tumors of the ovary, pelvic peritonitis, parametritis, and infiltration in the bowel,

tuberculosis, carcinoma and sarcoma, emphasize the importance of surgical removal.

Treatment.—The treatment is operative, since the literature clearly shows that medical and palliative treatment only aggravates the condition. Hysterectomy is the method of choice, since the growths are not definitely encapsulated and consequently cannot be enucleated, and because adhesions and adnexal disease are so common that conservative work is likely to be followed by an increase in adhesions.

OTHER FORMS OF ADENOMYOMA

Adenomyomata of the uterine horn and the round ligament, the broad ligament, the ovarian ligament, the ovary, and the rectogenital septum have also been described. In their essential features, they do not differ from the preceding types with the exception of the adenomyoma of the rectogenital septum. The adenomyomata of the round ligament are described under tumors of the round ligament (page 383).

Adenomyomata of the Rectovaginal Septum.—These are diffuse growths, consisting of nonstriated muscle and fibrous tissue containing small areas of mucosa scattered throughout a mass which is present in some part of the rectovaginal wall. They vary in size, although the majority are small. Heineberg, in 1919, reviews the literature and tabulates 47 cases. Cullen believes that they may start in the vaginal wall, just behind the cervix, and spread in a diffuse and irregular manner over the anterior rectal wall into one or both broad ligaments, until they finally present as a large mass to which are attached nearly all the structures of the pelvis. Clinically, they present in two types, one, the small tumor lying free in the rectovaginal septum, and the other which is firmly adherent to the pelvic organs, "binding them like glue." Heineberg believes that the nature and extent of the vaginal involvement does not bear any relationship to the size of the tumor.

The minute anatomy of these cases differs in no essential feature from the adenomyomata previously described. The chief interest lies in their symptomatology and treatment, since they may extend into the rectal wall or present in the vagina beneath the cervix, cause symptoms which may be confounded with cancer and constitute a mass, the removal of which presents considerable technical difficulty.

Lockyer states that the majority of students at the present time regard the tumor as an inflammatory product and not as a true neoplasm. Pick, Pfannenstiel, von Herf, and others favor the origin from the wolffian system, while FÜth, Kleinhans, Schwab, and others agree with Cullen that the gland elements are derived from the endometrium. Meyer, Raspini, Sitzenfrey, and Amann are among those who support the serosa theory.

Symptoms.—In addition to an increase in the amount and duration of flow, there may be bleeding from the rectum. Pain is common, as are pressure symptoms in the rectum. The pain is confined to the lower abdomen. The symptoms are increased during menstruation, and persist after the flow has ceased, features which should differentiate it from ordinary dysmenorrhea.

The *physical signs* are strongly suggestive. There is usually a dense nodular induration or a flattened mass present in the upper part of the posterior vaginal wall. The mass is usually closely adherent to the rectal wall. When high up, it is attached to the supravaginal cervix. Since the growth extends along the pelvic partitions, it involves the uterosacrals, broad ligaments, and ultimately presents as a dense pelvic mass, strongly suggesting cellulitis. The characteristic cysts are occasionally seen shining through the upper portion of the posterior vaginal wall. They may present as small, bluish points or project as polypoid masses. The vaginal covering may be lost and replaced by an ulcerating mass which bleeds easily. The rectal examination often gives a better impression of the tumor than does the vaginal. The rectum is often infiltrated and bleeds easily. There are yet no cases in which the tumor has penetrated the rectal wall.

Treatment.—The treatment is hysterectomy with the removal of as much of the infiltrated tissue as is possible. There is considerable question as to the value of removing part of the rectal wall when the tumor has invaded that structure. There are, in the literature, 10 cases in which areas from 4 centimeters to 20 centimeters in length were removed from the rectum, although there are many others in which there was no recurrence, even though small areas of the tumor were left in the infiltrated rectal wall. Sitzenfrey left an indurated bowel but no recurrence was observed even after ten years. He distinguished, however, between an adenomyositis of the rectum and a true adenomyoma of that structure and believed that the latter may develop on top of the former. As a result of his study, he concludes that the infiltrated type (adenomyositis) disappears after operation and, if there is no stenosis of the bowel, resection is not indicated. In true adenomyoma of the bowel, resection is indicated. Füh's case, and those of Kleinhaus and Moraller, showed the same benign characters even though a lump was left in the rectal wall. Rumpf's case of recto-uterine growth was well four years after operation without resection of the rectum and Glockner's case two years after. Meyer excised nearly the whole vaginal wall, which was riddled with gland tubules. The upper portion of the growth could not be removed, since it was so densely adherent to the rectum. Yet "cure occurred contrary to expectation."

As opposed to this conservative view, Cullen states that an early recognition of the growth is necessary if there is to be a safe and com-

plete removal. While the tumor lacks the characteristics of a malignant neoplasm, as evidenced by lack of metastases, and production of toxins, nevertheless, it menaces by the chance of obstruction of the ureters and rectum and the creation of dense adhesions in the pelvis, and also by its tendency to return after incomplete removal. Cullen advocates a resection of the rectum, together with the uterus, whenever the lumen of the bowel is greatly reduced, followed by anastomosis.

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CHAPTER VIII

CARCINOMA OF THE UTERUS; CLASSIFICATION; GENERAL METASTASES; SYMPTOMS OF CARCINOMA OF THE CERVIX

Frequency—Etiology—Cohnheim's theory—Parasitic theory—Symptoms—Disturbance of nitrogen balance—Heredity—Cancer families—Predisposing causes—Age—Classification of uterine cancer—Topographical—Histological—Morphological—Squamous-cell carcinoma of portio vaginalis—Everting type of cervical canal—Inverting type of cervical canal—Everting and inverting types of body of uterus—Adenocarcinoma of uterus—Cervix—Everting and inverting types—Method of extension of cervical cancer—The broad ligaments—Body of the uterus—Vagina—Pelvic peritoneum—Urinary system—Rectum—Adnexa—Lymph nodes—General metastases—Symptoms of carcinoma of the cervix—Percentage of operability—Leukorrhea—Hemorrhage—Clinical course—Diagnosis—Differential diagnosis—Prognosis.

CARCINOMA OF THE UTERUS

Carcinoma of the uterus is the most frequent tumor of this organ. Orth states that it forms 30 per cent of all carcinoma in women. It caused 14.3 per cent of the 31,000 deaths from malignancy in women in the United States in 1914. Roger Williams, writing in 1896, stated that one in thirty-five of all the women over thirty-five years of age died from uterine cancer in England and Wales according to the Registrar General's statistics. Kaufmann found that cancer of the uterus constituted 14.7 per cent of the cancers in both men and women in the Basle Institute, and 15.6 per cent of a similar series in Göttingen.

Frequency.—There is some difference of opinion as to whether uterine cancer is the most common cancer met in women, although the majority state that it is. Spencer quotes the 68th annual report of the Registrar General of England and Wales to prove that it is. During the years 1901 to 1905, 19,645 women died of cancer of the uterus in England and Wales, in contrast to 14,308 cancers of the breast and 12,048 cancers of the stomach. Birsch-Hirschfeld also placed cancer of uterus first in order of frequency in the malignant diseases of women in Germany. In Welch's statistics of 31,483 cancers of men and women, 29.5 per cent were uterine and 21.4 per cent of the stomach. The figures were all the more remarkable because the stomach cancers include those in both sexes. Roger Williams states that, according to his compilations, carcinoma of the breast is more common than uterine cancer. Dublin, collecting mortality statistics for the Metropolitan Life Insurance Company, found that, in the United States during the

six-year period—1911 to 1916—there were 3,666 cancer deaths, which constituted 5.9 per cent of the total mortality. Carcinoma of the stomach was most frequent of all cancers, 37.6 per cent of both sexes; cancer of the female genital tract caused 20.9 per cent of deaths of both sexes. It constituted 28.6 per cent of the cancer deaths in white women. From tabulations of 7,882 cancers in women, he found that cancer of the female genital tract was responsible for 25.3 per cent of the deaths per 100,000 in white women and for 37.9 per cent of the deaths per 100,000 in colored women.

Many believe that cancer is more common at present than it was formerly. Roger Williams' statistics show that 1 of 129 deaths from all causes in 1840 was due to cancer while, in 1894, it had risen to 1 in 23, an increase of more than 500 per cent. Wilcox's paper is interesting in this connection. It was based on a number of exhaustive reviews published since 1892, and included the excellent study of the Frankfort statistics of 1890 to 1913 by King and Newsholme. Wilcox states that the reported cancer mortality seems to be increasing in nearly every part of the world, but that the real mortality is not increasing with the rapidity which the statistics indicate. He feels that the apparent increase is due to improvements in diagnosis rather than to an actual increase, since cancer is now recognized in situations which were formerly inaccessible to study; and that a proper rearrangement of the older statistics so that they could be compared properly with recent compilations would explain away more than half, and perhaps all, of the apparent increase in cancer mortality. There are also other factors which merit consideration. It seems perfectly rational to believe that, since the mortality attending many infectious diseases which formerly amounted to plague has been greatly reduced, many more women nowadays live to the age at which they are liable to cancerous growths. The relative frequency of carcinoma of the uterus has been reduced in recent years because of better diagnosis in pelvic conditions. Sarcoma, myoma, carcinoma of the vagina and ovaries were formerly confused with carcinoma of the uterus. Now they are more likely to be recognized as clinical entities.

Etiology.—The etiology of carcinoma is not known. There are a perfect host of theories to account for the condition. Some are based on clinical observations, others on careful experimental work, and many are purely philosophical conjecture. In recent time, study of cancer is carried on by chemical and biological investigation both of the neoplasm and the general body metabolism of the host. The latter field, while relatively new, may later give promising results.

The theories which have been advanced to explain the origin of cancer come under a number of headings.

The older *theory of Cohnheim*, that cancer develops by the proliferation in an atypical manner of embryonic inclusion of epithelial elements, which

have remained dormant for a long period, has not received any support from histological studies. Yet it must be taken into consideration with nearly every theory, since the latter, as a rule, are most likely to come under the general heading of predisposing causes. The theory has not been accepted by Cullen and a number of other investigators, who have had much opportunity for studying both normal and diseased uterine tissues.

The parasitic theory has been advocated by a number of investigators who show that there are more points of similarity between cancer and infection than seem evident on casual reflection. Carcinoma runs a definite clinical course, becomes disseminated, and leads to constitutional disturbances, just as infection does. There is also a constant primary local origin, widespread metastases, and a definite predisposing condition which antedates the growth and diminishes the resistance of the affected parts.

The various predisposing factors are grouped as trauma, and may be of a mechanical, chemical, physical, or infectious nature. They are usually chronic. Maud Slye's experiments in mouse cancer at least indicate a transmissible predisposition for mouse carcinoma.

Direct contact infection is noted clinically in certain forms of cancer, as in carcinoma of the labia, which extends directly to the tissue of the opposite side with which it approximates; in epithelioma which has come on the lip of both father and son who used the same drinking vessel; in several undoubted cases of marital infection; by the frequent occurrence of carcinoma in certain localities, and often in certain houses. Moreover, the development of carcinoma which has been implanted secondarily during operation seems akin to infection which is disseminated in like manner. The advocates of the theory hold that implantation carcinoma in stitch-hole wounds of the abdomen, vulva or perineum resulting from cells which have been directly transplanted, indicates a lessened immunity to the development of the growth. They see the extension from cancer of the jaws to the vocal cords and lips as the result of transference of live tissues by a process comparable to skin grafting.

Advocates of the theory point out that all the specific diseases except carcinoma are admitted to be exogenetic. They state that their theory cannot be held invalid because the specific organism is not found, since the germs of many acute infections, as smallpox, etc., have not been discovered either. The majority believe that carcinoma is due to an ultra-microscopic organism conveyed in the tissues, and explain the different varieties of cancer which result on the ground of various reactions of various cells. Many have claimed to have found the cancer parasite, yet the Plimmer-blastomyces and Russell's fuchsin bodies and a number of other structures which were advanced as causal factors are now interpreted as degenerations of various kinds.

The probability that the various types of carcinoma are caused by a specific virus has received some confirmation by the work of Peyton Rous. This investigator obtained a filtrable agent which caused sarcoma in

chickens. The advocates of the theory state that immunity may develop to transplanted cancers in mice just as in infection, as has been proved by Clowes, Baesleek, and Gaylord in mice that have been inoculated with breast cancer. Some animals recovered with disappearance of the cancer, even though it had made an appreciable growth, and, for a long period after, they possessed an active immunity, shown by the fact that they could not be inoculated with the same tumor. Occasionally a definite, although slight, passive immunity was produced by the following experiment: the blood of a mouse, which had recovered after noticeable growth of a transplanted tumor, was mixed with a small portion of a similar cancer, incubated for a period, and then injected into another susceptible animal. Usually there was no growth. Immunity appears to develop more quickly if the cancer is injected in the spleen. Since splenectomized mice are more susceptible to cancer than are normal mice, splenic extract has been suggested as proper therapeutic means of combating the tumor.

The parasitic theory has aroused the very greatest interest, yet at present it cannot be considered as proved. The actual evidence which has been accumulated from the study of mouse cancer goes little further than to show that there are families of mice in which cancer occurs, and to prove that the disease can be transplanted from one mouse to another. Our present knowledge does not permit us to judge the extent to which observations of cancer in mice can be transferred to the problem of cancer in man.

There are several *theories* which have been *developed on purely philosophical grounds* that seem worthy of mention. One advances the view that carcinoma may result from an autoparasitism in which local accumulations of lymphocytes are important factors. It assumes that cell growth depends to some degree upon the action of lymphocytes, and that enzymes liberated from the nucleus are responsible for cell division. This is suggested by the fact that lymphocytes predominate in the blood during the period of most active growth, and shrink in number when the body has approached its potential size. The fact that the thymus and other auxiliary lymphoid tissues atrophy after the period of most active growth probably suggests the theory. Normally, the lymphocytes and their enzymes are held in check by antibodies. Thus they do not stimulate unduly cell division during chronic inflammations, although the lymphocytes are concentrated about the field. In case there is a loss of the lymphocytic control, because antibodies have not developed to a normal degree, as a result of hereditary or acquired factors, there would ensue a rapid proliferation of tissue cells with the formation of a cancer. The theory recognizes the two factors, local and general. Locally, the cells are stimulated by lymphocytes which have become concentrated around some local injury. The restraining influence of antibodies maintains a normal degree of cell proliferation. The general factor is a general loss of lymphocytic control, because of failure of the restrain-

ing antibodies which permits lymphocytes to carry cell division into a cancerous stage.

Another theory attempts to link cancer with the disturbance of the nitrogen balance in body tissue. It assumes that an excess of nitrogen compounds can cause an excess of cell division. It claims that nitrogen is liberated from the cell as a result of a stimulus of thermal, mechanical, or chronic nature. The nitrogen which thus escapes causes an increased instability of the protoplasm of adjoining cells which proliferate rapidly as a natural consequence. Carcinoma would be expected to develop more frequently in midlife, since the glands which control metabolism are undergoing alterations at that time. In case the functional activity of the spleen and lymphatics fails coincidentally, there results an accumulation of nitrogenous substances in the blood and body tissue which may permit an excessive cell division in tissues which have lost their resistance. Some have attempted to treat cancer on the basis of this theory. Shirlaw advocates the administration of spleen or lymph gland extracts, or their combination, as a therapeutic measure. This accords with the fact proved by animal experimentation that animals that have had their spleens removed are more susceptible to transplanted cancer.

Others have thought that an excess of sodium chlorid in the blood was responsible for the rapid proliferation of cells as far as the carcinomatous stage, and suggest the use of potassium nitrite in cancer to displace the sodium chlorid that is present in excess in the blood.

There is a difference of opinion as to the part which heredity plays as an etiologic factor. The older authors emphasized its importance, but in recent years it has been minimized, since it has not been found in a very large proportion of cases; yet we feel that one cannot spend years in hospitals and believe that family histories, as usually obtained, are of much value. Histories in the larger institutions are taken usually by very junior men from patients who in America, at least, know little of their family history. The patient is usually asked if there is tuberculosis, cancer or insanity in the family, without much explanation as to what constitutes the family. If cancer causes one of every seventeen deaths (Dublin's figures 5.9 per cent), it may well be that cancer families are often described to unsuspecting interns, since it is our experience that few hospital patients know the life history of a dozen members of their preceding generation. We believe, as a result of our study of cancer, that family histories taken in a correct manner will show that heredity may be an important factor, and that cancer occurs very frequently in some families, less frequently in others, and most rarely in the remainder, just as appendicitis does.

Tysser states that heredity plays a part in the general incidence of cancer in regard to species. Mammary tumors are comparatively frequent in mice, while they are rare in cattle. Cattle, however, frequently develop primary tumors of the liver and adrenals. He emphasizes the fact that statistical inquiries concerning the inheritance of a predisposition to cancer

in man lack accuracy, yet for the most part fail to indicate a tendency. He admits that cancer families are noticeably frequent, but states that many believe that they occur quite in accord with the laws of chance. He calls attention, however, to the fact that melanosis in the gray horse, and von Recklinghausen's disease appear to have heredity as predisposing causes.

The presence of cancer families in mice has been absolutely proved by the work of Maud Slye. There are numerous instances of cancer families in the human species. Sir James Paget mentions a family which suffered from carcinoma for three generations. Roger Williams cites a case of uterine carcinoma whose maternal grandmother, mother's sister, and two sisters all died of uterine carcinoma. Athill saw a carcinoma in a woman of twenty-eight, whose mother and two sisters also had carcinoma of the uterus. Guthmann saw a cancer of the body of the uterus in three sisters. Cullen reported 3 cases that were observed in sisters whose father died from cancer of the face. One of us (Lynch) saw a cancer of the corpus uteri in a patient whose sister died of carcinoma of the breast, a brother from cancer of the prostate, and the mother died from cancer of the uterus. We have, moreover, seen several instances of cancers in sisters, and 2 cases where the individual presented at the same time cancer of the cervix and cancer of the breast.

The percentage of frequency of the family history in uterine cancer series is given by the following authorities:

Gusserow	7.6 per cent in 1,028 cases	
Schroeder	8.2 per cent	Schroeder, Barker and Sibley series
Picot	13 per cent	
Williams	19.7 per cent	
Cullen	19 per cent in 176 cases	
Levin	8 per cent in 49 cases.	

The extent to which the family history was developed is not stated by any of the authors cited above.

Carcinoma is supposed to occur more frequently among the poor and ill-nourished members of society. Schroeder has supported this theory by statistics showing the relative frequency of fibroids and carcinoma. In his clinic, which is limited to the poorer class of people, fibroids were noted in the proportion of 100 to 61 cancers; in the wealthier class of cases, the proportion was changed from 100 to 332. These figures have been adduced to prove that the diminished resistance and impairment of vital growth favors the development of cancer. Yet the influence of habit and occupation is still a matter of uncertainty, and it has not been proved that carcinoma of the uterus is more common among the very poor than among the wealthy class. Roger Williams, among others, denies it and argues that his statistics show that it is more frequent among the rich. Older authors have stated that the disease is more frequent among those who eat meat than

in the strict vegetarians. We must remember, however, that the great majority of people are meat-eaters. The statement receives no confirmation in statistics of cancer in India, where the disease occurs in practically the same proportion in meat-eaters and in those whose religion prohibits the eating of any flesh. Self-indulgence in eating and drinking is more likely to be a factor which favors an increase in cancer mortality. Disturbances in metabolism from similar causes undoubtedly cause arterial degenerations.

Cancer is usually stated to occur more frequently in the colored than in the white races. Statistics from the Johns Hopkins Hospital confirm this opinion. The older idea that the disease was more common in temperate climates than in the tropics, and among the civilized races than among the uncivilized has been disproved by many observations in the Philippines. Dudley, in 1908, reported that carcinoma of the cervix is seen very frequently in Manila, where it is more common than any other type of cancer, and that the former impression that cancer in the tropics is very rare is not borne out by the facts.

Green found a definite relationship between the death rate of carcinoma and the type of fuel that was used for household purposes, and suggests that there may be some relation between coal and its products of combustion and malignant disease. He states that the death rate from cancer is high in northern France where coal is consumed almost entirely, whereas the death rate is low in southern France where wood is used largely for fuel. He believes that the cancer mortality varies almost in direct proportion to the type of fuel consumed.

There is considerable difference of opinion concerning local conditions which have been emphasized in the past as predisposing causes in the absence of true etiological factors of cancer. Cervical lacerations and erosions and other effects of child-bearing, and chronic inflammatory conditions of the uterus, are mentioned among these; yet they may be grouped under the general heading of chronic trauma. Great emphasis has been laid upon the relation between cervical lacerations and erosions and the development of carcinoma, although unfortunately there are no available statistics bearing upon this point. The importance of cervical lacerations has been mentioned by Ruge, Veit, Breiski, and many others. Theilhaber states that the anemia about the contracting scar favors the production of cervical cancer, just as it is supposed that the anemia following the menopause favors the formation of cancer in the body of the uterus. Williams states that he never found the disease in a tear in any of his cases, and feels that there is no evidence that lacerations play any part in the origin of cancer. Boldt, on the contrary, has found such a case, and there are similar instances, although they are few, which have been reported in the literature. Beckman observed a cancer develop in a cervical erosion in a case which he had treated over a period of five years. Such cases, however, are not necessary to emphasize the importance of cervical lacerations, since the secondary changes following a cervical tear may well suffice as an etiologic factor.

We have long believed that, if all the women who have had children, were to have their cervixes removed before the age of forty, that cervical cancer would be a comparative rarity. The point does not seem invalidated by the actual fact that early cancers have been found in the scar of cervical repairs in several instances. The chronic endocervicitis is undoubtedly of greater importance in the etiology than are the lacerations. Polese found that 34 of his 48 cancers had had a chronic endocervicitis antedating the tumor. In the absence of definite information concerning the etiology, it seems fair to emphasize again the importance of cervical injuries and inflammations. Routine examinations of chronic endocervicitis very often show abnormalities in the cell morphology and histology which may constitute precancerous lesions. We have no definite knowledge concerning the part played by previous inflammation as predisposing causes for cancer of the uterine body. Cullen was not able to find that an endometritis antedated the growth in any of the 16 cases with this type of cancer. Genital tuberculosis has been observed in association with carcinoma of the uterine body in many instances, as is shown by Coblentz, yet, as Cullen suggests, this relation may well have been accidental. Carcinoma of the uterine body is frequently associated with fibroids. Olshausen states that 10 per cent of fibroids occur with carcinoma. Taussig found a similar percentage in his recent review. There were 10 cancers of the uterine body occurring in 40 uterine fibroids in the Mayo Clinic. Levin was unable to confirm this idea in the analysis of his 613 collected cases, since fibroids were found in the uterus in 5 per cent of the cervical cancers and in but 1.5 per cent of the fundal cancers.

The great majority of cases occur in women who have borne children, yet occasionally carcinoma occurs in virgins, usually in those, however, who have had some pelvic condition which had been treated with a dilatation of the cervix. Sampson found that in 412 uterine carcinoma only 3 per cent were nullipara. Williams, in 334 cases, found that only 4 per cent were nullipara. Cullen, in 50 cases of squamous-cell carcinoma of the cervix, found that only 5 had not borne children; in 14 cases of adenocarcinoma of the cervix, there were 2 nullipara; in 19 cases of adenocarcinoma in the body of the uterus, 52 per cent had not borne children and 6 of the 17 married women had never been pregnant.

Age.—The great majority of the cases of uterine cancer develop about the time of the menopause. More are noted in the fifth decade than in any other ten-year interval. Cervical cancer is generally considered to develop earlier than that in the body of the uterus. Yet Levin, in his 1,613 collected cases, does not find any difference in the average age of the cancers of the uterine cervix and of the body. However, Wertheim has noted a large proportion of his cases of cervical cancer at an age much earlier than that usually noted for cancers of the uterine fundus. In his series of 500 cases, there were 6 per cent in women

under 30, and 30 per cent in women under 40, and 55 per cent in women 45 years and younger.

Williams, in 100 cases, noted uterine cancer as follows:

Before the menopause.....	50 cases
At time of menopause.....	21 cases
Past the menopause.....	29 cases

Gusserow, in 3,471 cases, found the following distribution:

Years.	Cases.	Years.	Cases.
17	1	40-50	1196
19	1	50-60	856
20-30.....	114	60-70	340
30-40.....	770	70 and over.....	193

Roger Williams, analyzing 500 cases, showed the following percentages:

Years.	Per cent.	Years.	Per cent.
20-25.....	.2	50-55	13
25-30.....	7	55-60	9
30-35.....	11	60-65	5
35-40.....	20	65-70	1
40-45.....	17	70 and over8
45-50.....	16		

A few isolated cases of cancer of the uterus have been reported in early life. Adams, in 1916, records a glandular carcinoma of the cervix and uterus in a child two and a half years old. Rosenstern found a case which he describes as carcinosarcoma of the cervix in a child of three. Glockner reports a cervical cancer in a child of seven. Engelhorn has collected several cases in very young subjects. Stacey observed a case of adenocarcinoma of the body of the uterus in a girl of sixteen. These are exceptions to the general rule, and there is a possibility that in other cases not cited in this chapter, the disease is really sarcoma. A case reported by Ganghofner was described as papillomatous and there is the possibility that it was not malignant. Green-Armytage, writing from India in 1913, states that he sees many cases of inoperable carcinoma in very young women. Of 9 cases which he treated by ligating the iliac arteries 5 were under thirty, and 1 was only twenty years of age.

CLASSIFICATION OF UTERINE CANCER

Much of the older study of uterine cancer is not of value for investigations at the present time, since in a single report there is often embodied a mass of statistics of both fundal and cervical cancers which are grouped together as if they were a single entity. This confusion, unfortunately, is maintained by a number of writers of the present day, who also discuss the various cancers of the uterus under this single heading without effort properly to subdivide them. Since cancers of identical histology and morphology may vary greatly in their clinical course, even though they arise from identical anatomical structures and location, it seems rational to believe that we will make slow progress in the elucidation of this confusing question unless we find a way of grouping similar cases. This, of course, means a very detailed classification. The chief objection to detailed classification thus far has been the fact that we cannot determine the proper classification for the majority of late growths. This objection is but theoretical, however, since our chief interest naturally must be the study of early cases, which at the present time are the only ones that permit the chance of cure. Fortunately, they allow much detail in their classification.

Carcinoma of the uterus may be primary or secondary. Following the rule that organs which are often affected with cancerous changes seldom contain secondary growths, we find that secondary cancer of the uterus is very rare. In 1908, Offergeld was able to collect but 22 cases after a very extensive review of the literature. The cases in his series developed secondarily from tumors which were primary in the stomach, breasts, and rectum. The tumors in his series which were found both in the myometrium and mucosa, had resulted from extension by way of the lymphatics, and had, in several instances, given off metastases from their uterine growths. This finding is somewhat at variance with that of Williams, who stated that the secondary uterine cancers were most often found immediately beneath the peritoneum of the uterine body. Both Williams and Offergeld agreed that metastases were usually multiple.

A number of classifications have been proposed for the arrangement of cancers of the uterus. They may be grouped from different standpoints, thus: (1) according to the site of the original growth; (2) according to the histology of the tumor; (3) according to the morphology presented by the cancer.

According to Topography.—Cancers may be divided according as they originate in the cervix or in the body of the uterus. In the same manner we may divide the cervical cancers according as they develop in the vaginal portion of the cervix, or in the cervical canal.

According to Histology.—There are two main divisions from the clinical and histological side: (1) the squamous cell carcinoma of the cervix; (2) the glandular carcinoma of the body of the uterus. This classification is the common one and has been used for many years. It has not obtained universal acceptance, however. Many, as Schottlaender, have claimed that any genetic classification is impossible, since both the cylindrical cell and squamous cell tumors can arise both from the cylindrical surface epithelium of the cervical canal, or from the squamous cell epithelium of the portio. Schottlaender further states that the additional term, round-cell tumor, has been introduced because of the limitations in this classification and urges the return to the rudimentary classification of uterine cancers into (1) solid growths; (2) primary glandular cancers; and (3) both the solid and the primary glandular cancers in combination. He takes into account the condition of the epithelial nests. Solid carcinoma do not have structures which suggest glands. They come from preëxisting squamous epithelium arising from the metaplastic cylindrical surface epithelium in the portio, and from the epithelial surfaces and the epithelium of the glands in the cervix, and the endometrium of the uterus. Solid carcinoma are divided further into ripe, unripe and midripe forms. The ripe type shows distinct prickle cells in individual cell nests, which feature is lacking in the unripe and midripe forms, irrespective of the presence of hornification. The midripe and unripe forms are differentiated according to the type of cell which is present in the growth. The unripe type contains small, round, irregular cells, in contra-distinction to the cells of the midripe tumors which are polygonal.

The objection raised by Schottlaender does not seem valid to us. It should be our aim to classify similar cancers so that we may learn the clinical and histological features of each of the various subgroups. Men working with cancer know that there are several different varieties of squamous cell carcinoma of the portio vaginalis, which vary in their habits of growth, although all of them may present identical features of morphology and histology. Advance will not result from simplification of classifications. We should carry our subdivisions down until there are only identical types of cancers in a single group. While this is not fully possible in any classification which has been advanced at present, the main classifications of topography, morphology and histology are proving extremely useful.

According to Morphology.—Cancer of the uterus may also be divided according to the morphologic features of the growth, irrespective of the situation or of its histologic structure. One definite type of tumor tends to evert as it grows, giving rise to a papillary, cauliflower-like mass. It stands to reason that this group will give symptoms fairly early, because the papillary masses are exposed to trauma which readily causes bleeding. The other group of cancers presents the same

histologic picture, but inverts as it grows and forms a nodular mass of cancerous tissue which tends to infiltrate the neighboring structures. It is readily apparent that this type of cancer may not give symptoms until ulceration occurs and a secondary hemorrhage results. The division into everting and inverting forms is not always frank, and occasionally both types may be present in the same specimen. Some cases show transition from one morphologic form to the other in the process of growth. Fortunately, however, the majority of early tumors permit this essential morphologic classification. Various synonyms for the everting form have been used, namely, everting, vegetating, papillary, and cauliflower. The inverting type is synonymous with contracting, infiltrating, nodular, ulcerating and parenchymatous. Either form may be further subdivided according to the nature of the predominating cell. When the tumor is soft, necrotic, or sloughing, it may be called medullary cancer. When the stroma predominates, the tumor is often called a scirrhous cancer.

Combining the above classifications, we shall consider the subject under the following heads: squamous cell cancer, and adenocarcinoma. Each form is subdivided according to its anatomical position, and further divided according to the morphologic features of growth.

Squamous cell carcinoma	{	A. Of the portio vaginalis	{	everting
				inverting
Adenocarcinoma	{	A. Of the cervical canal, arising from	{	surface epithelium { everting
				inverting
			{	cervical glands { everting
				inverting
		B. Of the uterine body, arising from	{	surface epithelium { everting
				inverting
			{	endometrial glands { everting
				inverting

SQUAMOUS CELL CARCINOMA OF THE UTERUS

Squamous cell carcinoma develops usually on the vaginal portion of the cervix, although it may arise in the cervical canal, or possibly even in the cavity of the uterus. It is the most common form of uterine cancer. Cullen found that 123 of his 141 cases of cervical carcinoma were of this type, and similar proportions are found in the larger clinics of America. Statistics from abroad give a somewhat different propor-

tion. There were 236 squamous cell cancers arising from the portio in 422 cervical cancers in Hofmeier's statistics. Baecker found that 282 of a series of 379 cervical cancers were also of the same type.

Squamous Cell Carcinoma of the Portio Vaginalis—EVERTING TYPE.—This form of cancer develops usually on the vaginal portion of the

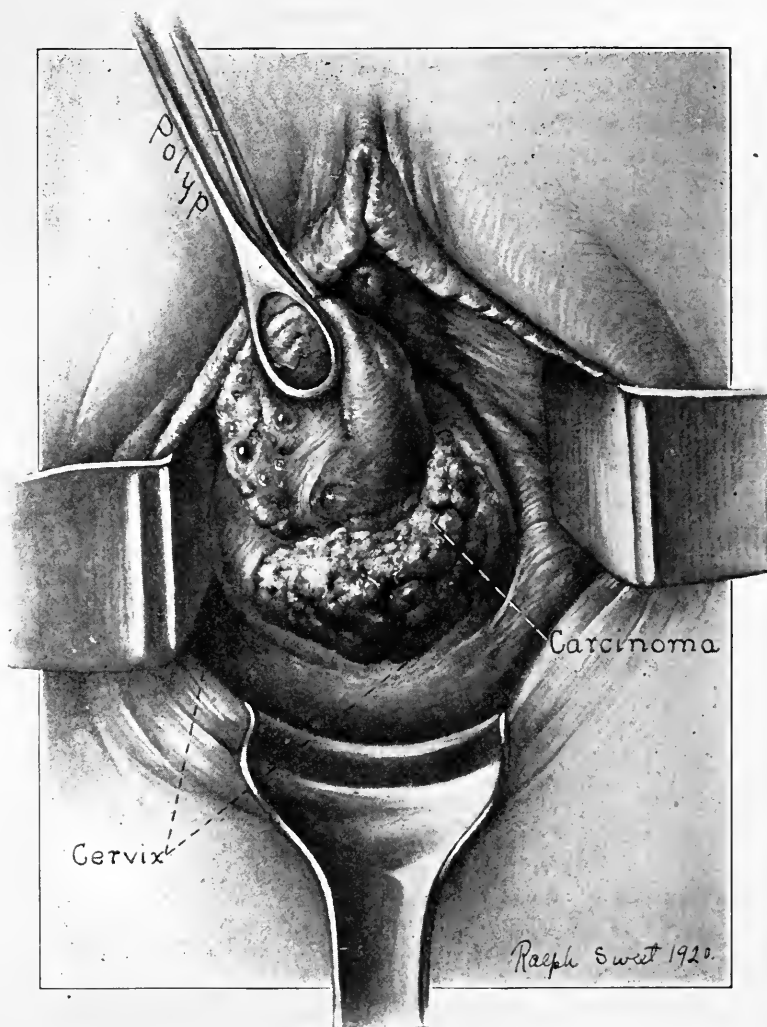


FIG. 58.—EVERTING SQUAMOUS-CELL CARCINOMA OF CERVIX WITH CANCEROUS POLYP.

cervix, external to the external os, and begins as a proliferation of epithelium which soon invades the underlying tissues (Fig. 58). Early stages are seldom seen, since they occasion no symptoms, yet they have been described by Waldeyer, Ruge, Veit, Cullen, Stone, and others. The very small tumor may appear as a diffuse, low, papillary outgrowth on the vaginal mucosa which bleeds fairly easily. The tissues immediately surrounding the

growth are slightly swollen. On section, there are a number of small papillae presenting a yellowish white and somewhat translucent appearance. With the progress of the disease, the tumor increases in size, covers the cervix with a cauliflower mass which may be sessile, or have a broad pedicle. The cervix becomes irregular and lobulated on the areas not covered by the growth. Superficial extensions occur in the cervix and in the upper part of the vaginal canal. Isolated nodules are occasionally found in the vaginal wall at some distance from the main tumors. The whole upper vagina may be distended with a large fungating mass. Ulceration comes on early and is followed by a slough which leaves wide excavations in the tumor proper, the cervix, or the vagina. The cervix is often completely destroyed, and rarely the growth may perforate into the bladder or rectum. It will be seen that this type of growth is very likely to give symptoms early. Leukorrhea is the initial symptom, and soon becomes discolored with blood, and later may be obscured by frank hemorrhage. In the early stages, the cancer is purely local, and since it expends the greater part of its energy in growing into the cavity of the vagina, it is not malignant in the sense that the inverting growth is. When the projecting polyp encounters resistance, it is stimulated to greater activity, and the tumor now grows back into the surrounding tissues. Unfortunately, the frankly polypoid tumors constitute a small per cent of the squamous epitheliomata of the vaginal portion of the cervix, and probably occur once for every 10 or 11 inverting cancers in the same region.

Microscopic Appearance.—In the earliest stages there is proliferation of the deepest cells of the surface epithelium which forms irregular branching columns and extends into the basement tissues. There is a cellular infiltration in the connective tissue which results coincidentally with or even precedes the epithelial invasion. There are different views concerning its interpretation. Ribbert claims that the cellular infiltration is the primary process and indicates some inflammatory condition, since it cannot arise from the epithelial proliferation alone. He found, in skin carcinoma, in the very earliest stages, a scab composed of horny cells and the secretion of sebaceous glands which he believes acted as irritant, from which he concludes that carcinoma originates as the result of subepithelial inflammation caused by epithelial products which diminish the differentiation of the epithelium and liberate the proliferated growth. Early stages of carcinoma of the cervix are rarely seen because the tumors may present no symptoms, and may be recognized only during examinations conducted for other reasons. The most common type is composed of pavement epithelium devoid of alveoli, and presents pearls, prickle cells, and hornification. True acanthomata are occasionally encountered. There is the typical hypertrophy of the squamous epithelium which presents elongated papillae which dip down into the underlying structures. The papillae, on transverse section, are round, oval, or irregular. Papillary outgrowths now appear

on the surface of the cervical epithelium. The projections of epithelium are soon provided with a delicate stem of vascularized stroma that extends up into the epithelial mass. The well-developed growth is comprised of cells arranged in columns of various dimensions. The cells are rounded, or polyhedral, or irregularly shaped, and occasionally there are giant ones. Usually the epithelial cells conform rather closely to the type of the parent cell, while at other times they deviate considerably even in early growths. Epithelial pearls occur, yet they are not nearly as frequent as in the epithelial tumors which develop in the skin, because of the scanty development of the stratum corneum in the cervical mucosa. The epithelium surrounding the growth appears normal, even as far as the very edge of the tumor, except for a round-cell infiltration which surrounds the growth. At the margins of the growth, the interpapillary processes are lengthened, and occasionally appear as long, slender, anastomosing cords. A zone of round cells surrounds the epithelial downgrowths. Eosinophils are occasionally seen. Degenerations are frequent in the older portions of the tumor and follow disturbance of the blood supply. There are cell inclusions of leukocytes, hyaline droplets, and even other epithelial cells. The principal degenerations are coagulation necrosis, fatty and hyaline changes, vacuolization and nuclear fragmentation.

INVERTING TYPE.—This type also begins as a proliferation of the epithelium of the vaginal portion of the cervix, but the papillary formation is absent or is evidenced to a comparatively slight degree. The tumor early inverts into the underlying connective tissues. The earlier stages may present as a hard nodule in the substance of the cervix. The lip of the cervix surrounding the growth is usually hypertrophied, appears livid and glazed, and is firm and infiltrated to the touch. There may be no other evidence of the tumor, since it develops in the connective tissue beneath the cervical epithelium. The growth occasions no symptoms at this time, and may escape recognition on casual inspection. As the disease progresses, there is likely to be necrosis in the central portion with a consequent production of a deep, ragged ulcer of typical carcinomatous appearance. Occasionally the tumor grows back into the cervix and may nearly surround the cervical cavity. Before necrosis occurs, the surface epithelium surmounting the growth may be thickened and puckered, suggesting the retraction so often seen in cancers of the breast. We have seen the entire cervical stump in this type of tumor washed off in the preliminary preparation for operation. In these cases, there must have been central necrosis in the tumor which had not extended to the surface. As the disease progresses, it invades the deeper tissues of the cervix, and extends directly outward into the paracervical tissues. Unfortunately, this inverting type of cervical cancer is far more common than the preceding, more malignant, and much more difficult to diagnose in the early stages. It may

present on the surface only a small, hard nodule, yet may have already invaded deeply the adjacent tissue. Occasionally the cancer may present as large nodular masses, when it is described as nodular cancer. As a rule, the process of invasion, necrosis and ulceration goes on together, when it is described as an ulcerative cancer. Clinical symptoms do not usually occur until the stage of necrosis and ulceration, and consist of bleeding and a serous vaginal discharge. It will be seen, therefore, that a cancer which undergoes necrosis at an early period gives symptoms sooner than one in which this process is delayed.

Microscopically the picture resembles that in the everting type of the squamous cell carcinoma of the portio vaginalis. Solid cell cords and cell nests are common. There is marked reaction of the connective tissues as a consequence of the ulceration. Changes in the endometrium are often found in association with the cervical carcinomata, varying from a glandular and interstitial hypertrophy with dilated glands, to an overgrowth of epithelium and cell reactions in the stroma. There may be an increase in the spindle cells and there is usually a round-cell infiltration (Abel and Landau). Krause has described the transformation of the cylindrical epithelium into a type resembling the squamous variety containing both flat and polyhedral cells.

COMBINING EVERTING AND INVERTING TYPES.—The combination of both everting and inverting types may exist, and the disease may begin as an inverting neoplasm which finally breaks through its shell and assumes the everting form. More commonly, the growth begins in the everting manner, but, encountering resistance which stimulates the cell proliferation, it begins to infiltrate. Papillary outgrowths may spring from the floor of an ulcer in an inverting growth. These variations do not impair the classification since, in combined forms, the growth must be classed according to the prevailing type.

Squamous Cell Carcinoma of the Cervical Canal.—This form of cancer is known to arise in the cervix, when the point of transition of the squamous cell epithelium into the columnar type occurs above the external os. It is a question whether it may develop from cylindrical epithelium which has undergone metaplasia and has been transformed into epithelial masses which resemble the squamous type. There may be everting and inverting forms.

The everting form in its development may come to fill the cervical canal and, encountering resistance, may grow downward and protrude through the external os as a polypoid growth. Extensions occur to the lateral margins and the tumor may extend over the vaginal portion and be indistinguishable from the type which arises primarily there (Fig. 60). If the mass occludes the cervical canal, pyometra results.

The inverting type which develops in the cervical canal occurs in the same manner already described for growths involving the vaginal

cervix. The cancer which arises within the canal first attacks the surrounding mucosa, and extends out on all sides into the cervical tissues. Infiltration and ulceration finally result, and the cervix sloughs away. There results only a thin shell surrounding the carcinomatous ulcer, which cannot be distinguished from later stages of the inverting type of epithelioma of the vaginal portion of the cervix. Very rarely necrosis may be deferred, and the cervix presents, on inspection, as a thick cervix covered with hypertrophied mucosa. The disease rarely invades the uterine cavity, and when it does, we are uncertain whether it extends by direct invasion or is carried by a metastases to the endometrium (see methods of extension, p. 196).

The diagnosis of this type presents all the difficulties which are encountered in the inverting cancers of the portio. It is clear from the above description that the diagnosis of the type may be made only in the early growths.

Squamous Cell Carcinoma of the Body of the Uterus.—The question whether the normal uterine epithelium surmounting the endometrium may be replaced by squamous epithelium has long been under debate. We often find in routine examinations, usually in association with pelvic inflammatory conditions, a heaping up of cells in the surface epithelium which suggests the beginning of a reversion to squamous cell epithelium. A number of investigators have reported such findings, notably Zeller, von Rosthorn, and Ries. Its rarity was emphasized by Ries who found in routine examinations of 200 uterine scrapings only 1 that had undergone this change. This is not in accord with our experience, since we frequently observe it. The question assumes importance in connection with the beginning of cancer. Are these changes in the epithelium purely the result of inflammation or are they indicative of precancerous changes? The finding of 3 primary acanthoma of the body of the uterus (Gebhard, Kaufmann, Flaischlen) strongly suggest the possibility that squamous cell carcinoma may arise as primary growths of the uterine body. The opponents of the view usually state that they are more likely to be secondary extensions from primary tumors of the cervix or that they have arisen from metastases. The 3 tumors adduced as primary, all appeared in elderly women. Others have noted that adenocarcinoma of the uterine fundus may show so many squamous cells that the tumor suggests a true adenoacanthoma. Some have even shown pearls; more commonly, however, the squamous cells appear in foci of the alveolar lining, and are clearly demarcated from the cylindrical epithelium. A combination of squamous cell carcinoma and adenocarcinoma of the corpus have been described by E. Kaufmann, who holds that there is a double origin from the surface epithelium which had been previously changed to the squamous type for one growth, and from the glands of the endometrium for the other.

ADENOCARCINOMA OF THE UTERUS

Adenocarcinoma of the Cervix.—Adenocarcinoma which produce atypically the alveoli of cervical glands occur in a small proportion of cases. The new growths may arise from the surface epithelium of the cervix or from that of the cervical glands. We cannot readily distinguish the frequency of the two types, since a differentiation is possible only in the very early cases. The tumors may be everting or inverting, although as a class they are distinguished by their power to invade the underlying tissues at a very early period. The everting growth, which arises from the surface epithelium, first appears as a proliferation of epithelium which soon presents a papillary structure. It grows into the cervical canal and extends along its course, although, at the same time, it deeply penetrates the cervical tissues. When the disease begins low down in the cervical canal, the cervical lips are soon involved and appear thickened, infiltrated and glazed. When it begins higher up, they are usually only hypertrophied on inspection, although they feel nodular to the examining finger. In a considerable number of cases, a cauliflower mass is finally extruded through the external os and presents a worm-eaten appearance because of the myriads of small, fingerlike polyps which spring from the surface. The cervix itself rarely bleeds from touch before there is a tumor which presents through the os. The polyp masses, however, are friable and bleed fairly readily, although not as easily as the everting squamous cell epithelioma. Ulceration usually comes very late. The entire cervix may be converted into a carcinomatous mass without noticeable necrosis or large areas of ulceration. Inspection of the tumor shows that it is composed of a mass of branching papillae, which consist of a stalk of connective tissue surrounded by several layers of epithelium. The carcinoma on section is firm and dense, and presents a yellowish white color which stands out in sharp contrast to the uterine muscle. Glistening bands of stroma may be seen on careful inspection. The tumor has an irregularly advancing margin. Microscopically, the growth begins by proliferation of the surface epithelium. The cells are heaped in an irregular manner, and soon assume the appearance of small glands, which are close together and are devoid of stroma. This picture rather suggests the squamous cell carcinoma. The connective tissue stroma soon grows in and branching papillae result. The stroma is composed of spindle cells and is relatively thicker and less vascular than that of the everting squamous cell carcinoma. For this reason, it does not break down as easily nor bleed as readily. The surface is covered by one or more layers of epithelium which present many variations in shape and size. As a rule, the cells are cylindrical when there is but a single layer. They are more likely to be polygonal when there

are several layers. There is, however, a wide range in their form and size. The nuclei are more apt to be large, round and vesicular, but vary in appearance and in staining properties, as do the cells. Giant

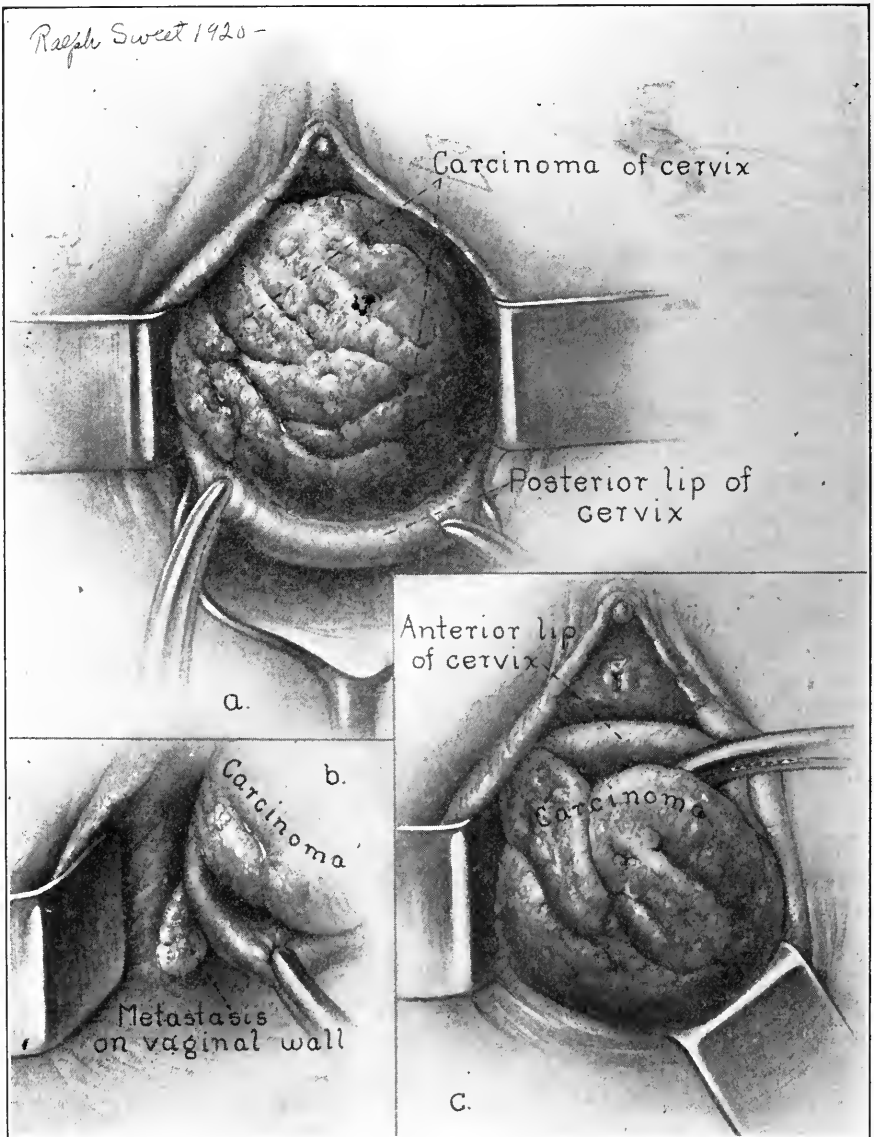


FIG. 59.—OCCLUSION OF CERVICAL CANAL BY A SQUAMOUS-CELL CARCINOMA WITH VAGINAL METASTASIS.

cells are often noted, and karyorrhexis is frequently seen. Round-cell infiltration accompanies the growth and is thought by some to suggest the degree of the malignancy of the tumor; its extent varying inversely with the malignancy of the cancer.

The inverting type of the growth is more frequent and arises more often from the glands than from the epithelium of the surface. It early inverts and is not likely to present the characters of the preceding type until the very late stages. In fact, the surface epithelium may be smooth or thinned out over a deep-seated nodular tumor. These growths early invade the cervical tissues growing out directly toward the parametrium. Consequently, the cervical lips may appear only hypertrophied or glazed and thickened until the very late stages. Palpation confirms this appearance, although it detects hard nodular



FIG. 60.—INVERTING ADENOCARCINOMA OF CERVIX WITH EXTENSIVE INVASION.

masses. Very rarely does a tumor grow down into the vagina or attain a size sufficient to fill its upper portion. It tends to grow directly laterally. Ulcer formation usually occurs only late in the disease. Leukorrhea is the early symptom, since bleeding may not result until the advent of ulceration. The diagnosis may be extremely difficult. Even after the uterus is removed, the growth may not be recognized until the organ is opened. Rarely a growth which has originated in the cervical glands breaks through into the vagina and assumes the polypoid type on its surface. Microscopically the tumor process may be best studied in glands. It may begin in the ducts or in the fundus

of one of the cervical glands. The cells proliferate at opposite sides, and become arranged in a number of small teats or club-shaped growths which gradually coalesce with their neighbors and form small cancerous glands. At one end of a normal-sized gland there may be a mass of cancerous tissue which completely occludes it, with a structure which appears to consist of a dozen or more newly formed cancerous glands with little or no connective tissue binding their lumen. The original gland shortly becomes filled and the cancerous tissue then invades the supporting structures. Occasionally, the early processes assume the characteristics of the squamous cell carcinoma, largely because of the scanty connective tissue framework. In the advanced forms the carcinoma may present as alveolar, diffuse or scirrhous. Occasionally tumors are found in which the lumina of the alveoli are completely obliterated, when the tumor assumes a solid appearance. The entire cervix may be invaded by glands which, on cross section, will show small offshoots with dentate branches forming new cancerous alveoli. Sometimes the growth can be traced from a normal gland which has been lined by a second layer of epithelium into the cancerous portion, where the cells are five or six layers deep, varying in appearance and in the staining reactions. Karokinetic figures are not uncommon. The cells differ greatly from those of the normal cervical epithelium, and cannot be recognized readily as their derivative. The surrounding connective tissue shows a round-cell infiltration which is usually more marked along the advancing edge. As in the preceding form, there appears to be an inverse relation between the extent of the round-celled infiltration and the rapidity of the growth. Degenerations are seen in the larger tumors and may progress to necrosis. The stroma occasionally presents a degeneration which resembles mucoid tissue.

Adenocarcinoma of the Body of the Uterus.—This type of uterine cancer will be separately considered (see p. 297).

CARCINOMA OF THE CERVIX

Method of Extension of Cervical Cancer.—The disease, unfortunately, does not tend to remain localized for any time, but, at a very early stage, depending upon the degree of malignancy, spreads to the surrounding tissues, either by direct extension, or by means of lymphatic and blood stream metastases. By these methods the cancer is carried to adjacent structures where it develops. The disease may extend in thick masses, or by thin threads of cancerous tissue, before the condition is recognized clinically as cancer.

The direct extension is most marked in a lateral direction, and the bases of the broad ligaments are first involved. The growth

soon breaks through into the lymph tracts, and groups of small cells are carried along in the current until they are arrested by the constricted lumen in the lymph nodes. From this point they back up until the new cells have gained volume sufficient to break out of the channels.

The broad ligaments are indurated in late cancers. The majority of authors lay much stress upon this sign as an indication of cancerous involvement, yet thickenings of the parametrium in connection with cervical carcinoma *may* be nonmalignant in character, and *may* represent only the absorption from the cancerous ulcer. This favorable condition, however, is not often seen. It is more important to bear in mind that invasion of the parametrium by cancer may occur without macroscopical change. Consequently, microscopic study is necessary to prove the presence or absence of cancer. This is well shown by an early series of Wertheim's in which the parametrium was involved in 60 per cent, while in another 14 per cent no cancer cells could be found by microscopical study, although there was considerable infiltration of the tissue. On the other hand, cancer was found in 22.5 per cent of cases, although the parametrium was soft and felt normal. The parametrium was found invaded by carcinoma in 75 per cent of Schottlaender's cases. Unfortunately, there does not seem to be a relation between the size and age of the primary growth and the involvement of the parametrial tissues. Occasionally, small tumors may invade in a very early period of growth, while larger tumors may remain local for a considerable length of time.

Carcinoma of the cervix rarely extends into the body of the uterus, and, in the few cases which do not follow the rule, the growth is generally confined to the musculature. Very exceptionally, cases are seen in which the whole inner surface of the uterine cavity has been involved by secondary extensions. Involvement of the uterine body may occur by means of the lymphatics, which run in the outer muscular wall of the uterus and anastomose with those of the cervix. It is found not uncommonly at a higher level in the myometrium than it is in the endometrium. The latter structure is occasionally invaded through its deeper layers by extension from processes in the muscular coat. At times the whole uterus is so involved that it is impossible to determine the origin of the neoplasm. Separate foci of cancer have been found in the endometrium at a considerable distance from growths which were primary in the cervical region (Jellett, Cullen).

The vagina may be invaded along the surface by direct extension (most common method), by way of the lymphatics in its muscular wall, or frequently by retrograde lymphatic metastases. It is involved in nearly 50 per cent of the operable cases, and is more apt to be invaded when the cancer begins on the vaginal portion of the cervix. In the everting type of growth, the metastases are usually very super-

ficial and spread by surface contact, although they are not well marked in all cases. The inverting type of the growth, on the other hand, whether beginning in the cervical canal or in the vaginal portion, usually extends to the vagina by way of the lymphatics.

The pelvic peritoneum in very rare cases may be involved at an early stage of the disease. Violet and Adler have reported such a case. There was a friable cancerous ulcer in a freely movable uterus and without evidence of involvement in the fornices. When the abdo-

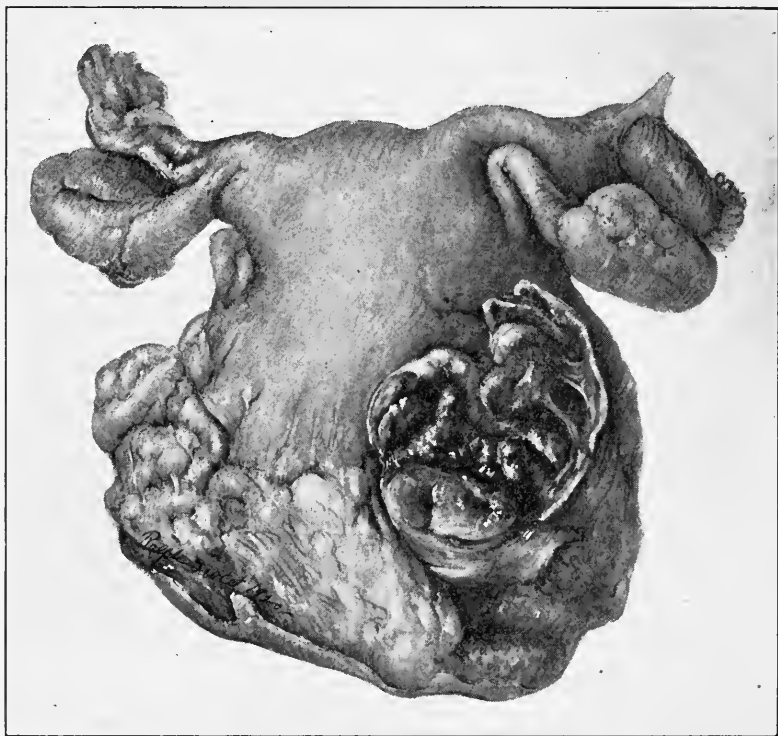


FIG. 61.—POSTERIOR VIEW OF FIG. 60. EXTENSION OF CANCEROUS MASSES THROUGH PERITONEUM OF RIGHT BROAD LIGAMENT.

men was opened, however, a large subperitoneal metastatic deposit was found in the subserous tissue of the lower part of the parietal peritoneum extending downward into the bladder; and, in addition, there were two isolated masses the size of a cherry which were found in the peritoneum itself.

THE BLADDER.—The muscular coat of the bladder is rarely involved, except in the very late stages of the disease. When the mucous membrane is invaded, nodules are found in the bladder, usually on the floor and behind the trigonum. Secondary necrosis of a cancerous extension may lead to the formation of a vesicovaginal fistula.

The ureters are frequently affected by the involvement of the parametrium or by extension from the base of the bladder. Compression of the lumen is common, although complete obstruction is rare. Hydro-ureter frequently results. Leitch found this condition in 75 per cent of his cases, and Albers-Schomberg in 40.2 per cent. Even in the operable cases, the results of this compression of the ureters may be so considerable as to interfere with the success of the operation. While Wertheim states that the ureters are extremely resistant to invasions, involvement is more common than is usually considered. As the pressure continues following the dilatation of the ureter, there is back pressure on the pelvis of the kidney which may progress to hydronephrosis. Infection of the bladder and ureters is common as a sequel of the operation, and pyonephritis may occur in consequence.

THE RECTUM.—The rectum is less commonly involved than is the bladder, possibly because of the protection given by the peritoneum of the posterior cul-de-sac. As the disease progresses, particularly when the cervical canal is involved, the growth extends along the uterosacral ligaments, and the wall of the intestines becomes infiltrated. Recto-vaginal fistulae follow the breakdown of carcinomatous extensions.

The ovaries and tubes are seldom affected. One or the other rarely may be involved by extension through the lymphatics. There are various channels through which this may occur; as through the lymphatics in the myometrium; more commonly by lymphatics along the uterine wall; and very rarely by a continuation of the growth to the lumen of the tube from the uterine cavity.

THE LYMPH NODES.—The uterine lymphatics vary considerably at different ages, and attain full development during adult sexual life, reaching their maximum during pregnancy and the puerperium. They are small and few before puberty, and after the climacteric they diminish progressively with advancing age. This latter factor is of clinical import, and explains the fact that corporeal cancer, occurring as it does so frequently in women past the menopause, grows more slowly and tends to remain localized for a longer period than does the cervical carcinoma which appears before the end of sexual activity.

There are different ideas as to the anatomical distribution of the lymphatics and their nodes. The lymphatics of the uterus rise from three channels, that is, from papillary networks in the mucous membrane, in the muscular coat, and in the peritoneum. Poirier and Cuneo claim that there is a connecting trunk which runs to the subperitoneal tissue, and anastomoses on the surface of the uterine muscle to form a fourth network. The plexus in the body and cervix is continuous without any demarcation between. There are no definite lymph channels in the endometrium, and the lymph flows in unlined spaces between the stroma cells. Occasionally, there are endothelial cells

which are found in the neighborhood of the uterine glands and on the walls of the blood vessels which may represent undeveloped lymph sheaths. There are many large lymphatic vessels in the middle and outer walls of the uterine musculature, which lie together with the larger blood vessels, and which communicate with the endometrium and the lymphatics of the cervix. The lymphatic vessels are noticeably smaller in the inner muscular layer.

There are six sets of regional lymph nodes of the uterus which may be involved by cancerous processes: (1) parametric; (2) hypogastric; (3) sacral; (4) lumbar; (5) iliac; (6) inguinal. Each group consists of from three to five individual lymph glands.

There are also a number of lymphatic nodules in the parametrium: (1) a definite node in the parametrium in the region where the uterine artery crosses the ureter; (2) a number of very small glands which are scattered through the parametrium; (3) a number of atypical nodes which seem to develop in the walls of the main lymphatics and protrude like a sponge into their lumen. The last group is most interesting and appears to be the reason why the outlying lymph glands are not more commonly involved.

Baisch describes a number of lymph channels which drain the portion of the cervix and the cervix proper, and which run laterally along the inner side of the uterine artery. He states that there are from five to eight of these, which properly group themselves into three sets, because they empty into glands in three different areas. The first empties into the iliac glands on the anterior surface and inner border of the external iliac artery, near the hypogastric artery which is the anterior branch of the internal iliac. The lowest of these nodes are also described as obturator lymph glands. The second set runs more posteriorly, and empties into the hypogastric lymph nodes on the internal border of the hypogastric artery. The third division arises more from the dorsal side of the cervix, and runs back over the posterior vaginal fornix to the uterosacral ligaments to the posterior pelvic wall, and empties into the glands by the side of the sacral ganglia, and occasionally higher up and more in the median line just beneath the promontory.

The lymph channels of the uterine body are arranged in four or five branches. They pass through the broad ligament beneath the tube but above the ovary, and run alongside the ovarian vessels upward and inward to end in the lumbar lymph glands just above the bifurcation of the aorta. In addition to these, the main branches from the uterine body, there are some lymphatics which arise near the middle of the uterus and join partly with the upper lymph tracts of the cervix. They finally pass along the round ligaments, and empty into the deep and superficial inguinal lymph glands.

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Due to the anatomical distribution of the lymphatics, the parametric, iliac, hypogastric and sacral lymph glands are the ones most likely to be involved by metastases from cervical carcinoma. These groups of glands are frequently designated as the first or lower group, since they receive the first cancer cells that are disseminated through the lymphatics. The lumbar and internal and external inguinal glands are usually termed the second group. They are more likely to be involved by the first dissemination of cancers from the body of the uterus, although they may be affected by cervical cancers, which have involved the first group with a dose so overwhelming that they spread through them and thence into the second group. Unfortunately we have no means of knowing, before microscopic study, when the pelvic glands are involved, nor the laws which govern metastases. Mention has already been made of the fact that very small cancers may give rise to early metastases, while large growths may remain localized occasionally for a very long time. It is usually stated that in the so-called operable cases, pelvic lymph glands are already involved in from 30 per cent to 50 per cent of cases. These figures were obtained by the microscopic study of glands removed at operation, and it may be that they are too low, since it is more than probable that many glands were overlooked which might have been cancerous, as the great majority of men remove only the large palpable glands. The following table shows the frequency in which the glands were found to be cancerous after operation, although cancers of the cervix and of the uterine body have been included by the authors in their series. This is most regrettable since, as we have already seen, cancers of the cervix differ markedly from those of the uterine body, both in their methods of invasion and their malignancy.

GLANDS FOUND CANCEROUS AFTER OPERATION

Authority	Per cent	Number of cases
von Rosthorn.....	42.4	28 cervical cancers
Wertheim.....	28	
Doederlein.....	33	
Bumm.....	33.3	32 cervical cancers
Sampson.....	64	27 " "
Pankow.....	28.2	70 cases (67 cervical)
Doederlein.....	22.8	115 cases (types not stated)
Kleinhaus.....	28	32 " " " "
Glockner (Zweifel).....	30	59 " " " "
Freund.....	25.8	
Schottlaender.....	43	Types not stated (presumably cervical)
Berkeley and Bonney.....	35	100 cases (types not stated)
Brunet.....	51	47 cases (types not stated, presumably cervical)

Cancer is found in lymph glands with varying frequency. Unless the entire gland is studied by serial sections microscopically, the disease may easily be overlooked. This has been well shown by Ries who demonstrated a very small gland which was cut in more than 300 serial sections. Cancer was present only on the last 25 slides.

The parametrium is usually affected before there is metastasis to the lymph glands. Indeed, it would seem as if the parametria had checked at least temporarily the extension in certain cases. The small gland near which the uterine artery is crossed by the ureter is involved in nearly all cases. Sampson has shown that the small discrete glands in the parametrium, which lie at some distance from the uterus, are also invaded nearly uniformly. Moreover, it would appear as if the lymphoid tissue, which hangs down in the lumen of the lymphatics, blocks a large number of cells in their progress toward the pelvic lymph glands. Kundrat observed this condition in 15 of 80 cases. Sampson found similar involvement in 4 of 27 cases, although distant metastases were present in 3 of them. On the other hand, the cancer cells may pass through the lymphatics of the parametrium without involving them, and not become lodged until they are arrested by the pelvic lymph glands. This has been proved by study of serial sections of the parametria. Sampson observed cancerous involvement by such study in 3 of 10 cases in which the parametria were free. Kundrat found that 10 per cent of one series of Wertheim's cases had cancerous lymph glands, although the parametrium was not involved. We have already alluded to the method in which the cancer grows about the lymph glands. The deported cells are swept along in the structures of the lymph glands until they are arrested by a small duct. Other cells come on from behind. Since they cannot pass further, they grow back in the lymphatic channels until they have increased to a mass of sufficient size to break through the channels and involve the neighboring tissues.

Cancerous invasion of the lymph glands can be proved only by microscopic study of serial sections, since the glands are usually enlarged from absorption of toxic products from the cancerous ulcer. They may be enlarged from other conditions, as tuberculosis. Schottlaender found enlarged tuberculous glands in 3 cases of his cancer series.

The older literature indicates that pelvic lymph glands are not invaded in a definite order. Careful work done during the last generation has proved that as a rule this is an error, although Sampson's finding is to the contrary. The majority, however, believe that the older findings were largely vitiated by grouping together of both cervical and uterine cancers, as well as by the mixture of autopsy cases with those that had been operated. Baisch has shown that metastases to the lymph glands in cervical carcinoma follow the physio-

logical and anatomical distribution, that there is no break in the chain, and that the second or remote group of lymph glands is not involved except in very rare cases when the first or lower group is free. Oehlecker, Vinay, and others have shown that the second group of lymph glands usually show a simple hyperplasia when the first or lower set are involved by a cancer. When the disease has extended completely through the first group, the second group also becomes carcinomatous. Baisch, in 52 cases of cervical carcinoma, which he studied, was not able to find one in which the lower and upper sets of lymph glands were simultaneously involved; nor did Winter, in 45 cases; nor Oehlecker in 7, except in autopsy cases, and in cancers of the uterine body. Leitch, who has investigated the records of 915 complete post mortems of cancer of the cervix, emphasizes the importance of the interiliac glands in the extension of cancer.

GENERAL METASTASES

The possibility of a general dissemination of carcinoma is not frequent in the early cases, and usually the patients die before there is a general metastatic invasion. There are, as yet, no large compilations which consider metastases in the various types of uterine cancer such as the portio vaginalis, the cervical canal, and the fundus. The value of the older tables is impaired because all types of uterine cancer have been included together. In 79 autopsy cases of uterine cancers, all groups, Williams noted the following sites of metastatic invasion:

	Cases
In the lung	7
In the liver	7
In the peritoneum and omentum.....	4
In the pleura	2
In the skin of breast and abdomen.....	1
In the tibia and innominate bone.....	1
In the heart	1
In the kidney	1

In 225 cases of uterine cancer of all groups, Blau, Dybowski, and Wagner found the following parts of the body were involved by metastases:

	Per cent	Cases
In the liver	9	24
In the lung	7	18
In the kidney	3½	9
In the stomach		4
In the intestines		4
In the thyroid		5
In the brain		1
In the adrenal		1
In the skin		1
In the gall-bladder		1
In the heart		1
In the breast		1
In abdominal muscle		1
In pelvic bones		1

Offergeld, in 1908, states, as a result of his study of carcinoma of the uterus, that metastases to the brain may occur relatively often. He collected 20 cases of metastases to the brain and 5 cases of metastases to the dura from the literature. He thought that metastases of the osseous system were determined by the blood system of the bone and its static peculiarity. Bony metastases occur by way of the arterial system, and rarely by retrograde venous transplantation. There was no evidence of osteoplastic formation, and the clinical symptoms of the bony metastases were identical with those produced by a tumor, that is, nerve irritation and the tendency for spontaneous fractures of the bone. He emphasizes the fact that occasionally men have been confused in their differentiation between the glandular involvement in advanced cervical carcinoma and general metastases. He found the favorite site of peritoneal metastases was the pouch of Douglas and the vault of the diaphragm. The secondary nodules in the omentum and the walls of the intestines originated from the lymphatics. Some of the peritoneal involvements did not cause symptoms; in the remainder of the cases, the complaints originated from the presence of the intra-abdominal tumor, chronic peritonitis, or stenosis of the bowel. The liver may be involved in from 5 per cent to 15 per cent of uterine cancers and the metastases may appear early or late. The involvement may follow through the lymphatics or hematogenous systems. It is favored by the double blood supply of the liver, consisting of the inferior hemorrhoidals, portal vein, and the hepatic artery. The lymphatic supply consists of radicals around the portal vein and tributaries in the pelvic and mesenteric lymph glands. Offergeld believed that liver involvement is not more frequent because the hepatic cells possess a biological fermentative activity which tends to destroy the cancer. Offergeld's review is painstaking and thorough,

and he divides, wherever possible, the primary growths according to their situation in the cervix and in the body of the uterus.

SYMPTOMS OF CARCINOMA OF THE CERVIX

The disease, unfortunately, develops in a very insidious manner. Proof that the symptoms of the early cancer are slight is shown by the fact that a large proportion of the cases are inoperable when first seen by the physician. The average duration of symptoms before therapeutic measures were undertaken in a large statistical series was six months. Others state that it is longer. Thus Farr found the average period from the onset of symptoms to the first consultation with a physician was 3.2 months in a series of 103 cases in New York City, and the average time from this time to their entrance into the hospital was 8.7 months. He obtained an average of 11.9 months from the onset of symptoms until the patient entered the hospital for active treatment. Farr's study emphasizes the point that because of many delays, patients in America seldom present for treatment while the growth is operable. Wertheim emphasized the fact that only 15 per cent of the cases presenting in his clinic in Vienna were operable when he first began his studies of cancer. In spite of the interest which has recently been created in cancer, less than 10 per cent come for treatment to our clinic in the stage that can be treated successfully by operation. The percentage of operability for carcinoma of the cervix varies greatly in the hands of different surgeons. Some men undertake to operate all cases, while others restrict surgical measures to the type of case which alone affords good chance of cure and do not believe in the so-called palliative operation. With this point in mind, we should study the following table:

PERCENTAGE OF OPERABILITY

European	Per cent	American	Per cent
Berkeley and Bonney.....	67	Peterson	20
Bumm.....	90	Jonas	50
Döderlein.....	68	Cannady	50
Franz.....	81	Smith	20
Jeannel.....	30	Janvrin	10
Krönig.....	87	Tate	15
Klein.....	40	Cunston	5
Kuestner.....	68	Frank	25
Lockyer.....	70		
Mackenrodt.....	92		
Mueller.....	89		
Polosson.....	56		
Reinicke.....	40		
von Rosthorn.....	36		
Wertheim.....	60		

The classical symptoms are leukorrhea and hemorrhage. These should be emphasized, since it is self-evident that the symptoms peculiar to late cases should not be considered when reviewing operable growths. Much of the confusion which exists in the minds of the general medical profession has resulted from the fact that operable and inoperable cancers are usually considered together.

Leukorrhea.—This is rarely the ordinary mucous discharge, but usually is a watery irritating discharge which may excoriate the vaginal mucous membrane and tissues with which it comes in contact. It is composed of serum, and may present the ordinary characters found in connection with endocervicitis. Leukorrhea was present in 75 of Waldstein's cases, and constituted the first symptom in 45 of 78 cases analyzed by Craig. Later in the disease, its color varies from yellow, brown, and green to bloodstained, depending upon the type of bacterial invasion. A characteristic fetid odor develops when ulceration has occurred.

Hemorrhage.—This is the first symptom noticed in about two-thirds of the cases, and may appear in women in apparently good health. Naturally, hemorrhage assumes greater importance after the menopause, since the great majority of women know that this is usually associated with malignant conditions. We believe, however, that changes in menstruation may be equally important, since Wertheim has shown that nearly 55 per cent of his first 500 cases developed while the woman was still in active sexual life (under 45 years of age). The bleeding comes from bursting of capillaries in cancerous nodules, and may follow a comparatively slight trauma, such as douching, coitus, or defecation. Quite naturally, everting growths call attention to their presence by means of hemorrhage earlier than do the inverting forms. There may be no bleeding from the latter type of cases until there has been widespread ulceration and extensive involvement of the uterus and parametrium. Occasionally the only symptom is a profuse and prolonged menstruation. Waldstein found atypical uterine bleeding as the early symptom in 120 of 219 cases, the symptoms consisting either of a slight flow between periods, or in an increase in the amount at the regular menstruation. Sampson stated that bleeding or a bloodstained discharge was present in 93 per cent of 412 cervical cancers in Kelly's clinic; in 60 per cent of these there was a history of bleeding for more than six months before the patient sought medical advice. Hemorrhage was the first symptom in 21 of 78 cases collected by Craig.

Patients frequently complain of *irritability of the bladder* as an initial symptom, and less frequently of rectal tenesmus. Vulvar irritation from the leukorrhea may also be one of the first symptoms of the disease. Pain is not an early symptom, and does not occur until the

uterine wall and parametrium have become infiltrated by the absorption from an infected ulcer.

It is unfortunate that the symptoms of this disease are not characteristic. Not uncommonly, the increase in nutrition and general well-being, which may follow the menopause, obscures the insidious onset. Even fairly intelligent and observant women are unable often to give a history of symptoms which date back more than a few weeks. The laity universally believe that cancer cannot develop without pain, and that irregular bleeding, and even hemorrhage, are characteristic of the menopause, an opinion which is readily confirmed by physicians who are not conversant with the disease. The only way to improve the mortality is to combat the ignorance which prevails concerning the early symptoms of the disease.

Clinical Course.—In the *very early stages* the patient's general condition is usually very good; indeed, a gain in weight is not unusual, a point already mentioned. Occasionally, however, the patient may complain of lassitude, loss of strength or weight, which, however, results more frequently from other conditions than from the early cancer. In the vast majority of cases the woman is not concerned over the appearance of a bloody discharge, attributing it to a reappearance of the catamenia, if the menopause has already occurred, or to the all-prevailing idea that irregularities or alterations in the character of the bleeding are normal consequences of the climacteric. The findings of examination in the early stages vary with the site and character of the neoplasm. The *everting carcinoma* will present only as a small polypoid excrescence, and rarely as a slightly raised broad plaque. The color of the growth is whitish and opaque, or else yellowish red. The consistency varies, but is usually less firm than normal tissue. It is friable and bleeds readily at the slightest touch. In the *inverting type* there may be only negative findings. The involved lip of the cervix is hypertrophied, and occasionally a hard mass may be felt within. The surface may be slightly granular, and induration and puffing may be the only feature observed. There is little tendency to bleed. In nearly two-thirds of the cases of cervical cancer which are operable, there is some ulceration, usually in the region of the external os. The border of the ulceration is elevated, irregular, and firm. The base is depressed, and is covered with small granular elevations, often surmounted with a grayish yellow exudate. The symptoms common to all ulcers are present, namely, discharge and bleeding.

When the disease begins in the cervical canal, the external os is patulous, and just within it may be felt the friable papillary excrescence or the hard, irregular ridge forming the border of a carcinomatous ulcer within the canal. The supravaginal cervix may be thickened and indurated, and beginning lateral extensions may diminish the mobility

of the uterus. Frequently, however, the parametric thickenings have resulted only from absorptions from the infected ulcer. If the neoplasm begins as a central nodule, the cervix feels hard and enlarged because of the carcinomatous area within its walls. If the mucous membrane is not involved, it may appear normal, yet, more commonly, it is fixed over the nodule and is puckered because of the induration.

The *second stage* represents the border-line case of operability. The ulceration advances, and there is considerable induration of the parametrium which fixes the uterus, usually to the left side. Hemorrhages are more common, and may come on without warning or may follow slight trauma. Vaginal discharge is present, at first thin, watery, and irritating, and usually with a disagreeable odor as a result of secondary infection of the ulcer. Even at this stage the patient's condition is good. Some look the picture of health, while others present anemia and loss of strength, if there has been frequent hemorrhage. Pain is usually absent, although discomfort or dull gnawing sensations are noted in the pelvis or back.

The *third stage* represents the inoperable condition. There is a marked impairment of general strength. The skin frequently, but by no means always, exhibits the yellow, white, cachectic appearance so characteristic of malignancy. Klemperer claims that this is due to the fact that more nitrogen is excreted than is received, largely because of the presence of infection. Hemorrhages are frequent and profuse, and a foul vaginal discharge is present in the intervals between the bleeding. Up to this point the symptoms are chiefly those resulting from the presence of an infected ulcer. With the extension of the growth to the neighboring structures, and with the involvement of the nerve sheaths, pain becomes severe. It may be either knifelike and darting, radiating to the hips, thighs, and calves of the legs, or occasionally only a steady, dull, constant ache in the pelvis. Involvement of the bladder is often ushered in by hematuria, when a cystoscopic examination may reveal carcinomatous nodules in the trigonum. Dribbling of urine generally indicates a vesicovaginal fistula, or a ureterovaginal fistula. When the growth spreads posteriorly, defecation becomes painful, and occasionally a rectovaginal fistula occurs. Colitis is a common sequela of fecal impaction and large quantities of mucus may signify its advent. Other intestinal symptoms, as nausea and vomiting, are frequent. Intestinal obstruction is not rare. Uremia threatens in the terminal stages, the intellect becomes dull, and edema of the face and extremities occurs. Fever is present from absorption of infected material from the ulcer and carcinomatous protein. Death may result from acute hemorrhage, but is more commonly due to some terminal infection, as pneumonia or septicemia, less frequently to multiple thromboses or extensive renal disease. Shortly before the end, the pain may become so severe that it cannot be controlled by morphine.

Diagnosis.—Unfortunately, the dictum, "the more certain the diagnosis, the less the probability of cure," holds true for all forms of

cancer of the uterus, and early diagnosis is the most important factor in the control of the disease. It is far better to regard all suspicious cases as malignant until proved otherwise. Delay often loses the patient the chance of cure by operation. A grave responsibility is laid upon the physician to examine thoroughly every suspicious case. The importance of microscopic diagnosis is emphasized by all authors, yet the great majority, unfortunately, do not qualify the method by which the microscopic diagnosis can be made. In uterine cancer, as in cancer in general, there is usually little difficulty in determining the fact that visible growths are malignant. Much harm may be done by removing tissues for microscopic sections in cancerous tissues, and delaying operation until the report of a pathologist may be obtained. Nearly every surgeon has long known that removal of cancerous tissue from the breast should be followed by immediate operation, if he would not lose for the patient the chance of cure, since the disease may be stimulated to most active growth by incision of its tissue. The careful surgeon, therefore, will not remove suspicious areas from a cervix unless they can be examined by frozen sections, and the diagnosis followed by immediate operation after the lapse of a very few minutes of time. All surgeons should bear in mind that at the present time we believe that only early cancers are curable by operation, and incomplete operations should not be attempted if the diagnosis is final.

Unfortunately, there may be no symptoms until a large craterlike ulcer has formed and the cervix is entirely eaten out by extensive involvement (inverting type of carcinoma). Suggestive symptoms, however, should be the indication for an exhaustive investigation. These are the following:

1. Intermenstrual bleeding or any deviation from the normal, particularly in women at the menopausal age who have borne children. Cervical carcinoma, however, may appear in young women who have not borne children.
2. Return of bleeding after the menopause has been established.
3. Bleeding after slight trauma from douching, defecation, or coitus.
4. Appearance of leukorrhea in a woman as a new symptom, or alteration in the amount and character of the previous vaginal discharge. Especially significant is a watery, acrid, or blood-stained discharge.
5. Pelvic pain. This is rarely an early symptom.

The findings of internal examination will depend upon the extent and location of the neoplasm. On the surface of the cervix or at the lower end of the canal at the external os, the tumor is accessible to sight and

touch; if the growth is situated in the upper part of the canal, the diagnosis is much more difficult.

The vulva may appear perfectly normal, although not infrequently, even in early growths, there may be evidence of irritation and excoriation of the skin, from an irritating cervical discharge. Vaginal examination usually shows the presence of a cervical enlargement. This may take the form of a prominent outgrowth extending above the general level of the surface, or the swelling may be in one wall displacing the external os toward the other side, or the entire cervix may be thickened. Naturally the cases which present at the external os and the vaginal portion of the cervix are more easily recognized than those which begin in the cervical canal. Rarely are the everting forms seen at the time when the growth consists merely of delicate, fingerlike processes. An important finding is hemorrhage which may come on at the gentlest touch. Yet it is important to remember that cases, in which the tumor develops in the cervical canal, or manifests itself as a nodular area either in this situation or on the cervix, may not bleed until the growth has so progressed that ulceration occurs. In addition to the hypertrophy of the cervix, the affected area usually loses its resilience, becomes hard, inelastic and boardlike.

As the growth continues, the vaginal fornix and the entire cervix may be the seat of a well-defined ulceration or a cauliflowerlike growth. The everting type of cervical carcinoma is the more easily recognized, because it gives symptoms earlier, but it is more rare, and usually is not as malignant as the inverting type, which ulcerates later, and consequently presents symptoms only in the more advanced stages. It is important to remember that there may be extensive inverting growths which appear to sight only as a small nodule, or as a limited ulcerated area either around the os or in the canal; and yet the disease may have progressed so far that the parametrium is already extensively involved. Sloughing later exposes the limits of the neoplasm. Occasionally, the appearance of the os will give us an idea as to the extent of the involvement, and the type of the cancer. Any puckering or retraction of areas on the vaginal cervix should arouse our suspicions, as should any nodules which are not nabothian follicles. On exposing the cervix, we find that it appears more glazed than the normal cervix. If ulceration is present, its color varies from a yellow to a greenish black, and the borders are raised, jagged and irregular. In the nodular type, the mucous membrane covering the surface usually presents a bluish, mottled appearance. When the symptoms point to a carcinoma which has not yet undergone ulceration, the cervical canal may be curetted, or a section may be removed from the cervix and studied by frozen section, provided only that the radical operation can be done immediately after the diagnosis of cancer has been firmly established.

Differential Diagnosis.—The following conditions may be confounded with cervical carcinoma: Congenital ectropion, eversion of the cervix, erosion, ulceration of the cervix associated with prolapse, simple hypertrophy of the cervix, lacerations of the cervix, cervical polypi, submucous fibroid polyps, tuberculosis of the cervix, syphilis of the cervix, condyloma of the cervix, diphtheritic patches, sarcoma of the cervix, retained portions of placenta, and endothelioma of the cervix.

CONGENITAL ECTROPION.—In nullipara it is not unusual to find a sharply defined red zone about the external os. It varies in width from 2 millimeters to 1 centimeter and appears to be continuous with the vaginal mucosa. This red color stands out in marked contrast to the bluish white appearance of the vaginal portion of the cervix. The area feels granular, yet there is no induration and no tendency to bleed. Microscopic sections show a normal cervix covered by a single layer of high cylindrical cervical epithelium.

EVERSION OF THE CERVIX.—This condition is akin to the preceding. It differs chiefly because the cervical mucosa has become everted by lacerations of the cervix. It is, therefore, found most commonly in multipara. The mucosa is bright red in color, and there is a clear line of demarcation between it and the vagina, although the outline is often irregular. This condition is often confused with ulceration, and is treated locally. In such cases there results a distinct proliferation of the cylindrical epithelium which is normally but one layer in thickness. There is no induration, nor does bleeding follow examination.

EROSION.—Properly speaking, this term signifies a loss of substance and should be limited to cases in which this condition is present. Erosions may be a precursor of carcinoma, and should be regarded with suspicion until their true nature is proved. Emmet years ago called attention to the fact that there are very few, if any, benign ulcers on a lacerated cervix.

ULCERATION OF THE CERVIX NONMALIGNANT, ASSOCIATED WITH PROLAPSE.—Simple ulceration is seen occasionally in prolapsed uteri when it results from the trauma which follows this condition. The cervix is usually hypertrophied, and the vaginal epithelium assumes the appearance of skin as a result of evaporation of the normal transudates and from the exposure to the air. There may be one or several ulcers which present a punched-out appearance and irregular contour. The ulcers are soft and the floor shows a typical granulating surface. They are readily dissected out and are very shallow. Rarely they are the seat of carcinomatous changes.

HYPERTROPHY OF THE CERVIX.—When the cervix is hypertrophied and studded with nabothian cysts and is the seat of a chronic inflammation, the condition may readily be confused with inverting cancers, especially if the cysts are large and lie in the depths of an enlarged and indurated cervix. In case of doubt, a microscopic diagnosis is indicated, made by frozen sections in the operating room. Occasionally under the microscope

the cervical mucosa is thickened, and presents papillae which are elongated and branching. There are, however, no downgrowths of epithelial cells which penetrate the basement membrane, nor are there mitotic figures.

LACERATIONS OF THE CERVIX.—Stellate lacerations of the cervix in early pregnancy, when the cervical tissue is smooth and soft and gives the appearance of being friable, may suggest carcinoma. Often on a gaping lacerated cervix one finds small papillary areas which are the result of an endocervicitis, and which at first sight may be confused with cervical cancer. The tissue, however, does not bleed readily. The microscopical picture gives the typical structure of the cervical endometrium.

CERVICAL POLYPI.—Mucous polyps projecting from the cervix may give rise to bleeding. The polyp itself is firm in contradistinction to the friable tissue of the carcinoma. Examination shows that they usually spring a short distance within the cervical cavity, and that the cervical lips are not ulcerated nor thickened as they are in malignant conditions. In case of doubt, microscopic diagnosis is indicated by frozen sections taken in the operating room.

SUBMUCOUS FIBROIDS.—A fibroid polyp lying within the cervical canal may present symptoms of hemorrhage, discharge, and tissue necrosis. Careful examination, however, reveals the character of the mass surrounded by the intact cervical canal.

TUBERCULOSIS OF THE CERVIX.—The symptoms of tuberculosis of the cervix may resemble closely carcinoma in the same region, since they result from the presence of an ulcer. Hemorrhage, however, is a less marked feature. Tuberculous ulcers are well defined and have undermined edges. The base of the ulcer is studded with nodules, is pale and anemic in appearance, and frequently is covered with caseous material. Induration is not as marked as it is in malignant conditions. Microscopic examination made by frozen section in the operating room will reveal the presence of giant cells and tubercles.

SYPHILIS OF THE CERVIX.—This may present in three forms:

(a) Primary chancres. These are rare, although not as uncommon as formerly believed. The ulcer is single and characterized by marked induration. There is little bleeding or discharge.

(b) Secondary lues. These lesions assume the form of broken-down papules. The ulcers are usually multiple, slightly elevated, and covered with yellowish necrotic material. They are usually associated with secondary lesions elsewhere on the body.

(c) Tertiary gumma. These are very rare and may simulate cancer, particularly if there has been much necrosis of cervical tissue. The ulcers in this condition are elliptical, sharply defined, and are usually covered with necrotic deposits. A routine Wassermann, done on all patients, will save much confusion.

CONDYLOMA OF THE CERVIX.—This is rare, but may be mistaken for evertting epithelioma. It is most often seen in pregnancy, when it may

resemble a cock's comb, consisting of a long base surmounted by many small, flat, epithelial outgrowths. It may be white or reddish in color. There is no induration. On microscopic examination the benign structure will be seen. The condyloma is a distinct papillary outgrowth from the cervix and is covered by normal epithelium.

DIPHThERITIC PATCHES.—These are very rare, yet may simulate a sloughing cervical cancer. There is usually elevation of temperature and other systemic disturbances which may suffice to establish the nature of the trouble. The Klebs-Loeffler bacillus can readily be isolated.

SARCOMA OF THE CERVIX.—This is an unusual condition and presents as a mass of polypoid grapelike structures, which are easily detached from the rapidly growing tumor. They may be very difficult to eliminate in the diagnosis without microscopic study. Both the circumscribed and diffuse varieties produce enlargement, hardening, and fixation of the uterus.

RETAINED PORTIONS OF THE PLACENTA.—Very rarely retained portions of the placenta which lie in the cervical canal after incomplete abortion and are associated with hemorrhage or infection, and the consequent necrosis, may simulate cancer. There should be little difficulty, however, since the history and elevation of temperature should suggest the true condition.

ENDOTHELIOMA OF THE CERVIX.—This is an extremely rare condition. Our knowledge concerning it, up to the present time, is based only on a few reported cases. The differential diagnosis between it and squamous cell carcinoma may be impossible clinically, and may present the greatest difficulties, even on histologic examination.

Prognosis.—The prognosis of cancer is death unless the condition has been removed by some surgical procedure. There are no reported cases of spontaneous cure, in which the diagnosis has been confirmed by the microscope, which have stood without recurrence for five years. Cancer may undergo spontaneous cure in other parts of the body, and Gaylord and Clowes have collected 14 instances, yet no case has come to their consideration which was of the cervix.

The average duration of the disease from the onset of first symptoms to death is from fifteen to twenty months, yet may vary widely because of many factors. Cancers differ markedly in malignancy, and great variations occur in the individual resistance of the patient. The adenocarcinoma of the cervix is usually much more malignant than the squamous cell carcinoma. Generally speaking, the inverting type of growth is more malignant than the everting variety, yet there are great variations in the individual cancers of the same general classification. Thus, there is a very malignant form of everting squamous cell carcinoma of the portio which gives metastases early and progresses to a speedy termination. On the contrary, there is a very slow-growing inverting form of adenocarcinoma of the cervix. Unfortunately, we cannot determine the malignancy of a growth by its histologic structure. The scirrhus forms are usually less malignant than

the medullary growths which present early degenerative changes. Cancers which are composed of cells of irregular size and form, and which present much evidence of rapid cell proliferation, are likely to be very malignant. We have already called attention to the fact that the duration of the disease may be modified by local conditions. Cancer is most malignant in the young, and the pregnant, and shortly after the puerperium, since the pelvis is usually hypervascular and the lymphatic structures most highly developed. It is of longer average duration when it develops after the menopause.

Cancer may, however, run a very rapid course. Kiwisch reports one case which progressed to death in five weeks, Martin one which lasted for nine weeks, and Henry Morris one of four months. The diagnosis in these cases was confirmed by the microscope. There are comparatively few cases in which the disease lasted for three years or more; Roger Williams was able to collect a number which formed 16 per cent of his collected cases. Rarely the disease may last for a considerable time when the case presents partial healing due to the development of cicatricial tissue which isolates the cancer cells and restrains their development. Barker has reported one case in which the duration was eleven years. Martin quotes a case of cervical carcinoma which was seen by him when it was a fairly extensive growth, and which remained alive at the time of his report, twenty-two years later, although the entire vault of the vagina had been transformed into a fistulous necrotic ulcer.

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CHAPTER IX

TREATMENT OF CANCER OF THE CERVIX; OPERATIONS; PALLIATIVE TREATMENT; RADIOTHERAPY

Historical sketch—Value of removing pelvic lymph glands—Operations for cervical cancer—Selection of cases for operation—Complications and contra-indications to operation—Operability—Choice of operation—Radical abdominal operation—Technic of Wertheim's operation—Drainage, complications—After treatment—Mackenrodt's operation—Bumm's operation—Paravaginal operation—Schauta's operation—Complications—Other operations for cancer of the cervix—Cautery amputation—Werder's cautery hysterectomy—Vaginal hysterectomy—High cervical amputation—Palliative treatment—General methods—Acetone—Percy's method of cauterization—Method of calculating operative results—Results of radical operation—Statistics—Of radical operations—Statistics of non-radical operative treatment—Treatment of recurrences following operation—Radio-therapy—Radium—Action of radium—Technic of application—Dosage—Screenage—Cross-fire—Complications of radium treatment—Results of radium treatment—In operable growths—In border-line cases—In inoperable carcinoma—In recurrences—Operation after radium treatment—Radium preliminary to operation.

TREATMENT OF CANCER OF THE CERVIX

The treatment of cancer of the cervix may be divided according to the stage of the disease, into three sections: (1) the earlier stages, in which the therapeutic measures are designed to cure; (2) the middle or border-line cases, in which the treatment aims to alleviate the symptoms, and possibly to cure; (3) the inoperable or terminal stage, in which the treatment is directed only toward the relief of suffering and the mitigation of the most distressing symptoms.

Historical Sketch.—Until comparatively recent times when the diagnosis of cancer was established, the condition was considered hopeless. Palliative measures only were adopted which consisted largely of curetting the ulcer and in cauterization. Very rarely, serious effort was made to remove the growth. As early as 1560, Andreas A. Cruce, of Granada, performed a hysterectomy with a cautery iron upon a carcinoma embodied in a prolapsed uterus. This method of treatment was followed by others, so that in 1,600 cases von Schenk was able to collect 26 in which there had been partial or complete removal of the uterus. In 1801, Osiander taught that amputation of the cervix should be performed as a curative measure. In 1813, Langenbeck performed a vaginal hysterectomy by enucleating a carcinomatous pro-

lapsed uterus without opening the peritoneum. Sauter, in 1821, divided the broad ligaments and ligated the uterine vessels with mass ligatures, and performed vaginal hysterectomy. With the advent of anesthetics, many surgeons attempted similar operations. The first advance in the principles of treatment beyond this point was advocated by W. A. Freund, who called attention to the fact that there was a definite advantage obtained by a laparotomy, inasmuch as the upper limits of the disease could best be appreciated. To facilitate exposure, he made use of the pelvic elevation which was subsequently popularized by Trendelenburg, and which is now commonly called the Trendelenburg position. By this method he removed a carcinomatous uterus by abdominal section on January 30, 1878, and six months later he was able to report 5 similar cases with 3 recoveries. Twenty-six years later he presented one of these cases at a gynecologic congress in Breslau and demonstrated the specimen which had been diagnosed by Cohnheim at the time of operation. There had been no recurrence up to that time, although his first patient died of recurrence one year after operation. Yet the immediate mortality attending Freund's operation in the hands of others was so high that it was not widely adopted. Ahlfeld, in 1880, found that the mortality of all recorded cases was 73 per cent, and Gusserow later collected 148 cases with a mortality of 71 per cent. The fact that freedom from recurrence was not frequent proved the greatest blow to the method, as was demonstrated by Rokitsansky, who, in 1882, collected 95 cases that had endured this operation with an immediate mortality of 65 cases. Of the remaining 30, there was not one that escaped a recurrence. The consequence was that operators turned to the vaginal operation which was then being developed by Czerny in Heidelberg after the method first proposed by Sauter. Czerny's first case was operated successfully on August 12, 1878. The following table shows the primary results from vaginal hysterectomy from the years 1880 to 1897:

Authority	Year	Cases	Per cent mortality
Heidler.....	1880	52	36.5
Olshausen.....	1881	41	29
Hahn.....	1882	48	29.1
Czerny.....	1882	81	32
Saenger.....	1883	133	28.6
Engstroem.....	1883	157	29
Kaltenbach.....	1885	257	23
Gusserow.....	1885	253	23.3
Sarah Post.....	1887	722	24
Schauta.....	1891	724	11.6
Hofmeier.....	1892	749	9.2
Hirschmann.....	1895	1241	8.8
Wisselinck.....	1897	1740	8

With the improvement in operative technic, others turned their attention to the development of operations after abdominal exposure. In 1881, Bardenheuer introduced vaginal drainage which, in a short time, reduced the primary mortality of abdominal hysterectomy from 70 per cent to 33 per cent. In the same year, Kolaczek, Reuss, and later Rydygier, called attention to the evil effects resulting from mass ligatures. Stimson, in 1889, advocated ligation of blood vessels after their isolation. Shortly after, Goffe, Polk, and Baer took advantage of Stimson's procedure, improved methods of peritonealization and emphasized the value of Bardenheuer's vaginal drainage and the necessity for the elevated pelvic position which was now called the Trendelenburg position. This resulted in a great reduction in the mortality attending abdominal hysterectomy, which nearly all agreed was the only method which permitted a proper inspection of the growth.

Ries, in 1895, proposed an operation which he had perfected upon the cadaver which aimed to remove the uterus, parametrium, upper vagina and pelvic lymph tracts in one piece. He emphasized especially the need of removing the pelvic lymph glands. In the same year, Clarke and Rumpf proposed and practiced similar operations, and emphasized the fact that it was necessary to isolate the ureters to obtain a proper removal of the parametrium. Numerous reports now appeared in the literature calling attention to the lack of cures after the older type of operation. They showed that metastases were far more common than had been believed and undoubtedly were responsible for the tremendous percentage of recurrences. Mackenrodt insisted upon the fact that the surgical removal of uterine cancer was not really started until the extirpation of the parametria began. Werder, in 1898, developed the operation which was subsequently proposed independently and popularized by Wertheim. Sampson, and others, developed operations which were even more radical, yet which almost without exception have been abandoned because experience has shown that they were too radical to be practical. Radical operations have been adopted very slowly, because the great majority of surgeons cannot bring themselves readily to perform operations which carry a high mortality.

The modern radical operation has been popularized largely through the work and writings of Wertheim. A painstaking study of the method of growth of uterine cancer worked out in many laboratories, as well as a careful consideration of the results following ordinary hysterectomy, have shown that a surgical cure can result only after all the ramifications of the growth have been removed. Laboratory workers have proved the uncertainty of clinical examinations; thus they have shown that a soft parametrium may be cancerous and that an infiltrated one may be free from cancer cells; also that carcinomatous lymph glands may be of normal size. Thus, Wertheim, in 1907, proved that, in 22.5 per cent of his cases, the parametria were soft on

clinical examination, yet were found by microscopic examination to contain cancerous deposits, and that carcinoma could not be demonstrated in 14 per cent of parametria which were thickened and infiltrated. The parametria and lymphatic glands were involved together in 20 per cent of his cases. Kundrat, in 1903, found that the parametria were free, but there was lymphatic involvement in 8 of his 80 cases. Cancer was found to be present in the parametria without lymph gland involvement in 27.5 per cent of cases. Kermauner and Lameris found the parametria were carcinomatous in 72 per cent of von Rosthorn's 33 cases studied in Heidelberg. Schauta, in 96 cases, found that one or both parametria were involved in two-thirds of his cases. Cullen reported that the disease had invaded the broad ligament in nearly every case of adenocarcinoma in Kelly's clinic. Kroemer proved the existence of carcinomatous invasion of the parametria in all of his cases. These, and similar studies, indicated the futility of operations limited to the removal of the uterus, since it was found that the growth had extended beyond the uterus in 60 per cent of cases which were deemed operable and that the actual condition of the parametria and glands cannot be determined by clinical examination. All, therefore, agree that all possible tissue in the neighborhood of the uterus should be removed. The necessity of excising the upper vagina together with the parametria is demonstrated by finding that four-fifths of the recurrences following ordinary hysterectomy have developed in the vaginal scar. Brunet found cancer in the upper vagina in 42.6 per cent of 47 of Mackenrodt's cases. With complete agreement as to the necessity of removing in one piece the uterus, parametria, and upper vagina, the discussion has become narrowed to the value of removing the lymphatic glands.

The Question of Removing Pelvic Lymph Glands.—Theoretically, the ideal surgical removal of a carcinomatous cervix should include the systematic resection of the entire cancerous areas and their avenues of drainage in one piece as advocated by Ries. Lymph glands which are cancerous are as dangerous as the original tumor. They are admittedly involved in from 30 to 50 per cent of early cases and probably in a larger per cent of the cases considered operable in America. Unfortunately, moreover, there is no clinical method of determining what cases present glandular involvement and the extent to which it has occurred. Yet it has been abundantly proved that no operation of any type can cure advanced carcinoma. Therefore, it is natural that there should be considerable discussion as to the value of removing the lymph glands, particularly if the attempt adds considerably to the mortality and proves ineffectual in the end. The evidence shows that the disease is hopeless from the surgical standpoint when it has extended beyond the parametria. There are some undoubted instances in which the patients have survived a five-year period of cure after removal of

carcinomatous lymph glands, but they are few. Many investigators (Olshausen, Hofmeier, Ott, Richelot, and others) insist that it is impossible to remove all the lymph glands at the operation. Post-mortem records have clearly shown that while carcinomatous lymph glands have been removed during operation, many others have been overlooked. Staude believed that extensive removal of the lymphatics is not possible upon the living subject, and demonstrated in 4 post-mortem cases that a resection of a portion of the mesentery would have been necessary in order to remove one single carcinomatous gland. It has also been claimed that posterior to the hypogastric artery there is a small gland which is frequently involved as demonstrated by post-mortem findings, but which, on account of its hidden position, cannot be palpated during operation.

The work of Schauta is often quoted by those who do not believe in the routine removal of the glands. He collected the glands from 60 post-mortem cases. They numbered 1,182 and were cut into 160,000 microscopical sections. For purposes of study they were divided into two groups, those accessible at operation (iliac and sacral), and those inaccessible (lumbar, celiac, superficial and deep inguinal). Both divisions were found involved in 35 per cent of cases. In another 8.3 per cent there was an involvement of the inaccessible lymph glands without involvement of the accessible group, so that removal of the accessible glands would have been valueless in 43.3 per cent of the cases, because the other set was also involved. In another 43.3 per cent of cases, both sets were free and in 13.3 per cent the accessible group were involved, although the inaccessible group were not invaded. Schauta concludes, therefore, that removal of the glands was indicated only in the 13.3 per cent because, in the 43.3 per cent it would have been unnecessary and in the other 43.3 per cent group useless.

Both Baisch and Wertheim have shown defects in Schauta's conclusions. Out of the 60 cases 50 were inoperable and should be ruled out of the discussion because only operable cases were being studied. Of the 10 operable cases, therefore, that remained, 8 were free from glandular involvement while in the other 2, both the accessible and inaccessible nodes were involved. These were too few cases to draw any conclusions. On the other hand, Baisch was unable to find a case in which both the upper and lower sets of nodes were involved in his study of 52 cases of cervical carcinoma. Similar findings were obtained by Winter, in 45 cases, and Oehlecker, in 7 cases. Unfortunately, Schauta does not mention the site of the tumor and Baisch suggests that probably carcinoma of the body was included in his series. In von Rosthorn's cases, the lumbar nodes were found involved in 9 per cent. Although Schauta's conclusions are not supported by subsequent investigations, his work is of interest, inasmuch as it showed that in only 43.3 per cent of his cases were glands involved.

Many have claimed that the lymph channels should be removed

with the affected glands or the purpose of the operation is defeated. Yet it is true that if the lymphatics are filled with cancer cells, operation is of no value. Sampson's work suggests that when cancer first invades the lymphatics, the growth extends as solid columns for a short distance, and that the glands become involved by small groups of cancer cells, which have broken away from the carcinomatous columns, and have been carried along the lymphatic currents to the hilum of the glands. Handley also demonstrated continuity of the cancerous growth from the primary tumor into the regional lymphatic channels, spreading centrifugally by direct extension, and largely independent of any washing away of cells. Cancer cells in the lymph tract have also been found by Kermauner, Veit, Schauta, and others. Their work emphasizes the importance of removing as much as is possible of the tissue lying between the primary tumor and the lymphatic metastases. Unfortunately, the removal of the glands may be the most formidable part of the operation, since they may be firmly adherent to the vessels on which they normally lie and, in efforts to remove them, the thin-walled veins may be torn through. Fatalities from this complication have occurred so frequently that the removal of the glands has been discontinued by most surgeons. Wertheim insists that removal of the glands is not as important as the removal of the parametria. Weibel, in 1914, stated that 25 per cent of Wertheim's cases were found to have involvement of glands and that all of them eventually succumbed to the disease. We have already alluded to Schauta's findings. Peterson removed 29 pelvic glands but only 5 were involved. Hofmeier, in 1911, states that the glands were enlarged in 46 of 90 cases. Only 18 (33.3 per cent) were carcinomatous. In no case in which the glands were involved was a lasting cure obtained. Ries and Bumm are the champions of the routine removal of glands in which stand they remain practically alone. They call attention to the fact that cancer always kills unless removed and that it is worth while to risk the serious procedure with a hope of curing occasional cases. Sampson's work shows that if the lymph glands have not been removed in the operable cases, cancer has been left behind in at least one-third and in possibly over half the cases. While it is impossible to remove at operation all the lymph glands which may be involved, we must realize that the more thorough and complete the operation, the greater the chance of curing the patient. Occasionally, cancer is arrested by the lymph glands. For these reasons, we believe that we should do the most thorough operation that each individual patient will stand.

Operations for Cervical Cancer.—As we have already indicated, the limit to which surgical operations may be extended has been fully reached. All agree that no form of operation may hope to cure late cancer, and that radical operation should be employed only in early cases. The trend of opinion is that all others should be radiated. There are few dissenting voices to the belief that ordinary vaginal or

simple abdominal hysterectomy should never be done. The surgical principles for the treatment of cancer of the cervix are identical with those which obtain for operation of cancerous organs elsewhere in the body. The fundamental principle should be block excision of the entire cancer field in one piece, including the area of lymphatic distribution and drainage. Practical considerations, however, especially those of primary mortality, permit one to limit the operation to wide removal of uterus, tubes and ovaries, broad ligament and parametrium, vagina and paracolpium, in one piece. Practically, however, no operation can ever be devised for the treatment of cervical carcinoma which will be ideal. From the very nature of things, considerable trauma must attend any operation which seeks to remove tissues from the depths of the pelvis, since they never can be brought to the surface of the wound without much traction. The radical operation is attended with considerable primary mortality, for which reason many still perform limited operations, thus losing for the patient a rational chance of permanent cure. Some have decried the radical operation because it is so difficult technically that it should not be performed by the majority of men in active surgical practice. We cannot believe that this is a valid objection. There is abundant proof that the operation cures when more limited procedures fail. It is our firm belief that the situation will not be improved by simple ablation of the uterus through the vagina, or by simple abdominal hysterectomy, as is now done in the great mass of cases throughout the country. Both the laity and the profession should be educated to know that cancer invariably kills unless it is removed completely and that nothing is gained for the patient by an incomplete removal.

Selection of Cases for Operation.—In order to obtain good results, cases must be selected carefully for operation. The vagina should always be carefully examined to detect cancerous nodules. These are recognized without difficulty when they are elevated above the surrounding mucosa, but, if they exist as flattened plaques, they may be easily overlooked. Next the broad ligament should be examined to determine the presence of induration, yet it is important to remember that a soft parametrium may contain cancer cells, and that parametric thickening and induration may be due only to an inflammatory change. We should constantly bear in mind that the condition of the parametrium does not always indicate the extent to which the cancer has spread, yet it is apparent that a growth which has left a large ulcer is likely to have involved the parametrium. The uterosacral ligaments should be carefully palpated. This is best done through the rectum. The presence of enlarged glands along the sacrum should be carefully sought for. Beadlike irregularities along the course of these ligaments strongly suggests carcinomatous invasion, yet induration may exist here from a previous endocervicitis associated with old lacerations. The condition of the local uterine growth must be taken into considera-

tion in estimating the chance of parametric invasion. If the tissues about the cervix are normally soft, the cancer presumably is still local. On the other hand, if there is an extensive local growth with indurations extending along the pelvic walls on one or both sides, sufficient to fix the uterus, there is every reason to believe that the parametria are involved and the case is at least at the border line of operability. The majority of men believe that this type of growth is best treated by radium. Bumm stands almost alone in recommending operation.

The general condition of the patient and her past history may aid in arriving at an opinion as to the nature of the induration, yet the local growth is of primary importance. When the disease has spread down to the vagina, or has involved the bladder or rectum, either with or without the formation of fistulae, the disease is quite hopeless. Cystoscopic examination occasionally aids us in determining whether the bladder is involved. Pale, edematous patches of the vesical mucous membrane, especially in the region of the trigonum, usually indicate that the wall of the bladder has become infiltrated by the cancer. Their presence does not absolutely contra-indicate attempt for radical operation, although it often causes failures. When the vesical wall is infiltrated and contains yellow-white circumscribed nodules, the viscus is definitely involved, and the operation should not be undertaken, since experience has absolutely demonstrated that it will not accomplish cure. Occasionally, the bladder mucosa which overlies the cervix is pale and wrinkled, and suggests infiltration of the underlying musculature. The greatest care is necessary in separating the bladder from the uterus at operation in this type of case. Fromme, in 1908, was unable to detect any changes in the interior of the bladder in 65 of 110 cases of carcinoma of the cervix, and in all of them he was able to effect a separation of the bladder at operation. He found vesical edema in 15 of his cases, and regarded it as an evidence of bladder involvement, since the bladder could be freed from the uterus and cervix only with much difficulty. Cruet reviewed the report of 500 cystoscopic examinations made on cancer of the cervix. As a result of this investigation, he concluded that simple bulging of the bladder wall was not of diagnostic significance, but when the floor is thrown up into deep folds with intervening valleys, that there are adhesions between the bladder and the cervix. While these do not constitute an absolute contra-indication to surgical procedure, they limit the chance of cure. Such cases, we believe, are better treated with radium. Cases which present edema of the bladder wall must be regarded as inoperable. Before the advent of radium into the therapeutic field, there was not complete agreement among various authorities as to other points which render the case inoperable. The ureteral orifices may be pushed to one side, or may be diffusely red with edema, without contra-indicating operation, although it indicates a border-line condition. When the ureteral orifice is enlarged and flattened, and especially when it

protrudes as an edematous area into the bladder, the condition is inoperable because of bladder involvement. Some hint as to the involvement of the bladder wall may be given by study of the urine spurting from the ureteral orifice. The interval between the spurts is longer and the jets appear more forcible on the involved side.

When a case appears border line, operation is justified in the absence of radium. Yet it must be of an exploratory nature until the surgeon is sure that there are no metastases which contra-indicate it. The under margin of the liver, especially near the gall-bladder, should be inspected, the vault of the diaphragm palpated for peritoneal metastases, the pelvic glands should be carefully palpated, the broad ligaments minutely inspected and the lower uterus viewed with the idea of determining whether the growth has involved the bladder wall.

Complications.—Various conditions may be present, some of which absolutely contra-indicate operation. Among these may be mentioned serious heart disease, nephritis, pyelonephritis, diabetes, tuberculosis and other systemic diseases. Even though the local condition appears operable, such cases are far better treated with radium.

There are a number of other conditions which merely complicate the operation. Chief of these is pelvic inflammatory, which occurs so frequently as almost to constitute the rule. Not infrequently, the pelvic inflammatory disease may be so extensive that in itself it constitutes a serious condition. Such cases cannot be treated with radium.*

Occasionally *carcinoma* may arise in a *double uterus*. Valentine and Buist have collected 5 cases in which carcinoma was present in a double uterus with a double vagina, 4 of which had a cervical cancer and the other a cervical cancer and a cancer of the uterine body. Rossa describes a case of a multiparous woman of thirty-eight, who had a bicornuate uterus with a cancerous cervix which had caused atresia of the vagina and consequent pyometra.

Fibroids may be present with cervical carcinoma, although the association is not as frequent as in cancers of the fundus. Kerr found only one cancer of the cervix in 200 abdominal hysterectomies for fibroids, although he found 6 cases of cancer of the uterine fundus in the same series. The relative infrequency of cervical cancers in fibroid uteri is all the more striking, since cervical cancers are from fifteen to twenty times more common than cancers of the uterine body. Others state that cervical cancers occur with fibroids in less than 5 per cent of cases, whereas cancers of the uterine body are found in nearly 30 per cent. Some, as Eden and Lockyer, explain this variation on the ground that cancers of the fundus occur on the average in older women than do cancers of the cervix. In this connection, the statistics of Wertheim are of interest in that 6 per cent of his 500 cases occurred in women of thirty years and under and 55 per cent occurred in women of forty-five years and less.

Tuberculosis of the uterus is sometimes observed as a complication of cervical cancer. Schottlaender, and Cullen, each have observed a number of cases in their own series. Delval and de Halluin have added others to the list.

Pyometra often complicates the operation, even in operable growths, so frequently in fact that large tenacula may not be safely used to elevate the fundus during operation. Atresia of the cervix is responsible for the greater number of cases. The fluid may be clear and serous, may contain pus, or may be bloodstained. It is malodorous, often extremely fetid, and varies in quantity from a few drams to a pint or even more. Stein, in 1910, found this condition most frequent in women in advanced life, since it usually occurs in an organ which has undergone atrophy. Walter Tate noted it 3 times in 28 cases, and Bürkel found it 17 times in 273 cases, or 6.2 per cent. Many cases present no symptoms, although it is quite possible that the condition is overshadowed by pain resulting from parametric infiltration. The majority, however, complain of pain, either alone or in association with a purulent discharge. As a rule, there is no temperature reaction, nor general symptoms.

Pregnancy in association with cervical carcinoma constitutes a very grave condition. Fortunately, it is rare, although it is rather surprising that it is not more often seen, since cervical carcinomata were noted 29 times in women under thirty years in Wertheim's series of 500 cases. The disease progresses most rapidly because the congestion of the pelvic tissues and the marked development of lymphatics favors early extension.

Operability.—The percentage of operability for a number of European and American surgeons is given below. In studying this table, we should bear in mind that, in the future, the operability undoubtedly will be reduced, since only early and local growths will be selected for operation. Others will be treated with radium.

The relation of the operability and primary mortality is shown by the following table:

Operator	Percentage operability	Percentage primary mortality
Jeannel.....	30	35
von Rosthorn.....	36	13.6
Doederlein.....	48	14.3
Klein.....	40	12.8
Reinecke.....	41	21
Polosson.....	56	18.7
Wertheim.....	50	18
Franz.....	81	19.28
Bumm.....	90	20
Mackenrodt.....	92	19.2

Graves, in 1921, emphasizes the fact that, in the past, operability has meant that the surgeon could remove the growth, whereas in the future the term "operability" will be restricted to cases where the growth may be removed with hope of cure.

Choice of Operation.—There is a very general opinion that the abdominal operation is preferable to that done through the vagina, whether the glands are to be removed or not, since the best exposure is gained by laparotomy. Schauta, and Staude, on the other hand, claim that when the paravaginal incision is used the vagina, rectum, and bladder are more accessible than by the abdominal method. Certainly, the best exposure is obtained for the vaginal and parametric removals. Yet there have been a number of cases reported in which carcinoma was implanted in the vaginal wound. Jayle, in 1909, reported severe disturbances from the vaginal cicatrix of the paravaginal incision. Reports, moreover, are indicating that the ultimate results are not as good as those of the abdominal route. Certain it is that the paravaginal operation is one that may not be successfully undertaken by a surgeon who has not carefully developed this trying technic. Mackenrodt, and others, believe that the paravaginal operation is more complicated and dangerous than the abdominal one.

Undoubtedly, both types of operation have their advantages for one who is conversant with the technic. Now that radium has become the accepted treatment for all except early and clearly localized growths, it may be that revision of our older ideas concerning the advantages and disadvantages of each type of operation is necessary. In choosing between the paravaginal and abdominal operation, it is important to remember that, if the glands are involved, the prognosis is very poor. Postoperative shock is not as common after the paravaginal operation as following laparotomy, a point worth remembering, if the case is very fat so that exposure would be difficult through an abdominal incision. Accidental injuries are just as frequent in both types of operation. Injury to the ureter may be better treated from above, although unfortunately such injury is seldom recognized until the development of complications. With the passing of Schauta, the paravaginal operation has lost its great exponent.

RADICAL ABDOMINAL OPERATIONS

At the present time there are two general types of operations: one in which the surgical measures are restricted to the removal of the uterus, adnexa, parametrium, and the upper vagina; the other is more truly radical, in that it attempts to remove all the tissues in the pelvis which may be involved in the growth of the disease. The first type is represented by the operation which has been popularized by Wert-

heim; while the other is exemplified in the operations of Ries, Mackenrodt, and Bumm.

The Wertheim Operation.—This operation is essentially that of Werder, and differs from it only in a few details of technic. It merits the name Wertheim, because Werder has abandoned the operation, and Wertheim, by his persistent work for twenty years, has done much to put the surgical treatment of carcinoma on a sound basis. The operation differs from the older methods of Ries, Strumpf, and Clark, in that the systematic removal of the lymph glands is not attempted.

The patient is put on a light diet twenty-four hours before the operation. The pubis and abdomen are shaved and prepared on the afternoon preceding the operation. The prepared parts are protected with dry sterile dressings. On the morning of operation a soapsuds enema is given, which is followed by a vaginal douche of $\frac{1}{2}$ per cent lysol solution. Preliminary to the anesthetic, she is given $\frac{1}{4}$ grain morphin and 1/100 grain of atropin.

There is considerable discussion as to the best type of anesthetic. Many surgeons advocate lumbar anesthesia, yet it is usually found in America that women of the better class are not so readily made insensitive by this method. This method of narcosis has the very great objection that it does nothing to prevent the patient from experiencing the horror of being awake during an operation which may last two and a half hours or more. The advocates of lumbar anesthesia claim that it is superior to inhalation anesthesia in cases presenting heart or kidney complications. We are of the firm belief, however, that operation is not wisely done on patients with heart or kidney complications. They are best treated by radium.

Disinfection of the Vagina.—Opinions differ as to the extent and the proper time for preparing the cancerous ulcer. Krönig emphasizes the modern trend when he states that he fears curetting, because it may disseminate the carcinoma cells into the deeper structures, and because those already present cannot be destroyed by this method. He merely sears the growth with the actual cautery just before the abdominal operation. Bumm favors curetting the day before the operation. He attempts to break down all cancer structures with a sharp curette, and sears the surfaces with a Paquelin's cautery. Personally, we feel that a preliminary treatment with radium ten days before the operation is a very great aid to the treatment, provided it may be done without anesthesia, since cancer cases do not usually do well after two anesthetics in close sequence. We feel that no matter what is done, the cancerous ulcer cannot be freed of the myriads of pus organisms. We advise cauterizing lightly as the first step of vaginal preparation just preceding operation. The vagina is then cleansed with green soap and water, irrigated with a solution of $\frac{1}{4}$ per cent lysol, which is followed by an irrigation of 70 per cent alcohol. A

vaginal pack is now inserted firmly against the carcinomatous ulcer. Previous to the insertion of the pack, the bladder is catheterized. Neither the instruments used nor the room in which the preparation is done should be used for the operation. The patient is then placed flat, and the abdomen is prepared for operation by cleansing with alcohol, ether, and $\frac{1}{2}$ tincture iodine solution.

Abdominal Incision.—There has been considerable discussion as to the type of incision which will secure the best exposure. It has been our experience that the ordinary midline incision from the symphysis to the umbilicus is most satisfactory. Some, as Bumm, cut transversely some of the lower mesial fibers of the recti muscles; others, as Mackenrodt, make a horse-shoe incision through the skin and all the other abdominal layers. The incision runs a couple of finger breadths above the anterior pelvic brim. Following the opening of the peritoneum, the skin, fat, and peritoneal edges should be protected from carcinomatous cells or infected material by properly draping the margins of the incision so that no part of the abdominal wound is left exposed. We see nothing but disadvantages in suturing together skin and peritoneal edges. The patient is placed in the elevated pelvic position as soon as the anesthetic has taken effect, and before the abdomen is opened. This facilitates the packing off of the intestines, since they have had time to accommodate themselves in the upper abdomen. Heavy rubber dam pack, about thirty-six inches square, is excellent for holding back the intestines. Self-retaining retractors give satisfactory exposure.

Separate Steps of the Operation.—The upper abdomen is inspected and searched for evidence of metastases. They may be found on the liver, near the gall-bladder, or in the omentum. They cannot well be located on the vault of the diaphragm. The broad ligament should be carefully palpated to determine its condition, and definitely trace the extent of infiltration. The glands at the bifurcation of the common iliac vessels should next be palpated. If they are of normal size they can scarcely be felt. The glands on the anterior surface of the sacrum are next palpated. If the cancer is present as a cancerous ulcer, the glands are likely to be enlarged, but this does not always mean carcinomatous invasion. The uterosacral ligaments are now traced to their attachments in the wings of the sacrum. The cancer extends out from the uterus more commonly on the left side. If it appears that the disease has spread so far that the entire growth cannot be removed, the operation should be abandoned. A simple hysterectomy should not be undertaken.

The fundus of the uterus is elevated by two heavy clamps placed on the upper margins of the broad ligament in order to avoid the chance of breaking through the uterus in the presence of a pyometra. The uterus is pulled toward the symphysis and away from the broad liga-

ment which is to be first opened. The ovarian vessels are now tied doubly with chromic No. 2 sutures, after which the round ligament is tied close to the pelvic wall. A crescent-shaped incision is made in the broad ligament from the ovarian vessels, through the round ligament, to the vesico-uterine fold of peritoneum in the midline. The loose connective tissue of the broad ligament is now separated from the pelvic walls by blunt dissection. The connective tissue strands run in the general direction of the ureters and large vessels, and they should be separated carefully so the important structures will not be injured. The ureter usually lies attached to the median fold of the broad ligament, and may usually be exposed readily by opening up the connective tissues with long hemostats. On account of the danger of necrosis, which Sampson and Fickel have shown may follow the destruction of the vascular network, the ureters should not be isolated above the structures which are to be removed, and their capsules should not be stripped away. The uterine vessels now come into view, since they run in a direction transverse to the broad ligament connective tissue. The uterus is now pulled high into the abdomen, and the detachment of the bladder from the cervix is completed as far down as the insertion of the ureter. By passing a clamp along the sheath of the ureter, the uterine vessels are isolated, and the branchings of the superior vesical artery may also be brought into view. It is best not to attempt to tie off the uterine vessels until the ureter is exposed nearly down as far as the bladder. Wertheim advocates pushing an index finger of one hand down along the ureter and toward the bladder to isolate the uterine vessels. This, to us, seems unnecessary trauma. Inflammatory changes in the broad ligament often complicate the dissection, and there is a likelihood that there are dense adhesions to the ureter. The same condition is often met with after preliminary radium treatment. Much fat in the depths of the broad ligament is another unfavorable condition, and great care is necessary to keep from getting into the wrong strata.

Ligation of the Uterine Artery.—If the blood vessels and ureter have been exposed according to the method described, there is usually little difficulty in ligating the uterine vessels. These vessels cross the ureters transversely. In tying off the uterine artery we must avoid ligating the superior vesical artery. The uterine artery and the superior vesical artery originate, as a rule, in a short common trunk from the hypogastric artery. For this reason, one should not tie too closely to the hypogastric artery, but select a place rather mesial to the branching of the superior vesical artery. Should the vesical artery be tied, gangrene of the bladder may follow. If the blood vessels be tied too close to the hypogastric artery, secondary hemorrhage may occur. Bumm has reported such a complication which resulted fatally. The uterine vessels are tied with No. 2 chromic catgut, and it is impor-

tant to be absolutely certain that the ureter is not included in this ligature. At this step it is necessary to determine whether or not there is another deep uterine vein lying immediately beneath the ureter. If this is present, there may be abundant hemorrhage from it, since it is easily injured, and in attempting to clamp it, other hemorrhages may arise by further injury to the adjoining venous plexuses.

Exposure of the Ureter to the Bladder.—The uterine vessels have been tied as close as one dares to the large vessels of the pelvis. The ureter is now elevated from its parametric attachments and traced to its

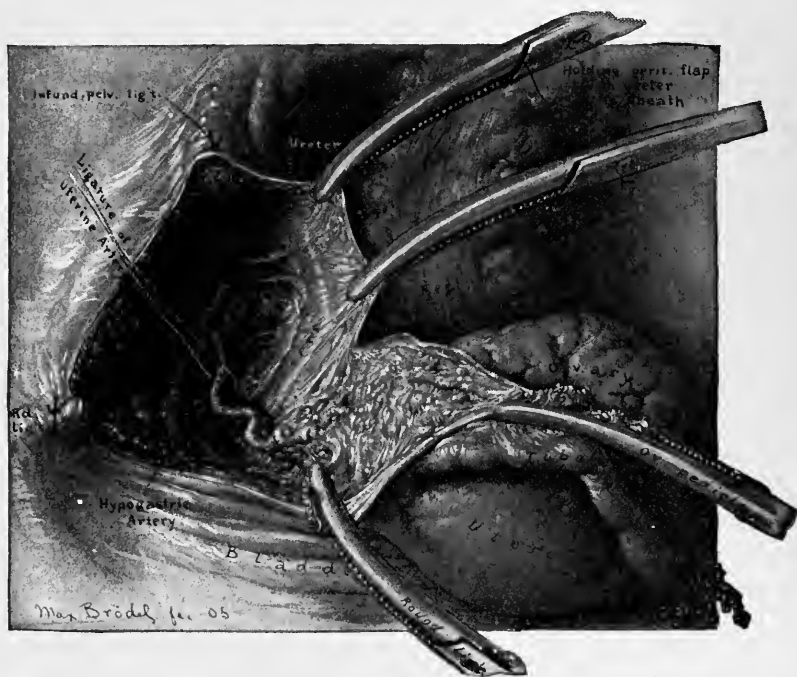


FIG. 62.—EXPOSURE AND LIGATION OF THE UTERINE ARTERY (Sampson). The exposure of Bumm and Mackenrodt is identical with this procedure (Kelly, *Operative Gynecology*).

insertion in the bladder. This may cause much difficulty from a technical point of view, since the facility of the isolation depends upon the extent of carcinomatous infiltration. If one elevates the uterine end of the severed uterine artery and draws it toward the uterus over the ureter, it can be demonstrated that the ureter is attached to the cervix by thin bands of connective tissue. These bands may be cut without difficulty or risk when they are put on slight tension and defined by raising the uterine artery. The connection between the vessels and the ureter being severed, the latter can be worked out of its parametric bed. The vessels with the lymphatics and glands remain in contact with the uterus. There is a small gland

until all the arteries leading to the uterus are ligated. When the extirpation has been completed, it will be found generally that the bleeding has ceased or may be controlled by a few clamps with comparative safety when the uterus has been removed and all essential landmarks are in plain view.

Incision of the Posterior Peritoneum and Separation of the Rectum.

This should not be attempted until both ureters have been isolated through their entire extent, and the bladder has been separated from the cervix. The peritoneum posterior to the uterus is cut from one ovarian pedicle to the other. The uterus should be drawn to the symphysis before this is attempted, since it elevates the pouch of Douglas. Usually the peritoneum can be pushed off by blunt dis-



FIG. 64.—REMOVAL OF THE PARAMETRIUM FROM UNDER THE URETER (Sampson; Kelly, *Operative Gynecology*).

section. In our practice we seize and elevate the rectum, and separate the peritoneum and connective tissue from the rectum with dissecting scissors. We believe that this is the most important step in the operation, since it should be our aim to remove all traces of the pouch of Douglas. The rectum is now separated from the vagina, which can usually be done by blunt dissection. The uterosacral ligaments are now exposed on their mesial sides. The rectum is freed as far back as seems safely possible, since it should be our aim to remove the parametrium from the actual pelvic wall.

Extirpation of the Parametrium.—It is a good rule to attack the better side first, since the mobility of the other is increased and the excision is usually made easier after one side has been extirpated. Wertheim has advised right angle clamps to close off the carcinomatous crater in the vagina during this step of the operation. They are widely used, but to us have many objections, chief of which is that

they obscure the field in the depth of the pelvis. If a heavy curved broad ligament clamp be placed on the sides of the paracervical tissue and traction exerted, the roots of the parametrium will be seen to run out in broad masses when they may be excised from the pelvic wall by blunt or sharp dissection. The excision begins at the anterior parametric roots which are exposed by holding the bladder upward and outward, while the operator makes strong traction on the vaginal clamp. When the anterior part of the parametrium is severed, which may be done with comparatively little bleeding, one may work along the sides laterally and out from the rectum, and peel the connective and fatty tissues as far as the posterior root of the parametrium. It is well



FIG. 65.—RAW SURFACES AFTER REMOVING UTERUS AND PARAMETRIUM.

at this stage to place heavy broad ligament clamps on the uterosacral ligaments close to the pelvic bone. They contain vessels which may cause troublesome bleeding. Incision is made under direct sight with the ureter in full view. Care should be taken that the rectum is freed far enough down so that the upper half of the vagina is in full view. The vagina may now be incised under direct sight, cutting from the side while an assistant seizes the vaginal stump with mouse-tooth hemostats, so there may be no overflow of purulent fluids into the raw bed created by the operation. As soon as practical, all raw surfaces should be walled off with gauze to prevent contamination. Often the cul-de-sac is obliterated by adhesions; there may be difficulties in sufficiently freeing the rectum. This, however, is the most important step of the operation, and the operation will fail if at least the upper third

of the vagina is not removed. The two vaginal edges are brought together and closed from the sides with interrupted sutures of chromic No. 2 gut. After the vagina is closed, assistants change their gloves, and the instruments which have been used during the operation are discarded, since they have become contaminated.

Extirpation of the Glands.—This is the last step of the operation before closing the peritoneum. Theoretically, it is more correct to begin the operation from the brim of the pelvis, and to remove all the lymphatic tracts and ducts as one works down toward the uterus. This, however, constitutes a tremendous operation by itself, and should not be attempted by men first trying the radical operation. Ries writes that he often takes from an hour to an hour and a half before he is ready to do the hysterectomy. The majority of men extirpate only the enlarged glands, which is not a logical performance, beginning at the periphery and working down from the bifurcation of the common iliac artery. There are many bleeding vessels which must be tied, and often there is difficulty in freeing inflammatory glands from the large veins.

Closing the Peritoneum.—The method of closure depends upon whether there is subsequent drainage. All agree that the anterior peritoneum should be sewed to the anterior flap of the vagina with interrupted catgut sutures. This aids in the hemostasis for the bladder wall, and aids in its support. It is also an important step in preventing paresis of the bladder and the subsequent cystitis. The lateral angle of the vagina must be sutured with care, and attention paid particularly to hemostasis and avoiding the ureters. The rectum is now supported by attaching the posterior peritoneum to the posterior vaginal wall. The raw surfaces in the pelvis have been greatly reduced in size by this procedure. The floor of the parametric stumps should be dry and without oozing. Absolute hemostasis is necessary if one desires to close without drainage. In such event the peritoneal margins are united with a continuous suture from one infundibulopelvic ligament to the other. If the peritoneum is scant and cannot be closed without tension, interrupted sutures should be used. Or if closure is impossible in this manner, the sigmoid may be brought across the pelvis and sutured to the anterior bladder flap so that the pelvis is cut off from the abdominal cavity. The vagina may now be tamponed with gauze as firmly as possible to make pressure upon the parametric wounds as far out as possible.

Drainage.—The great majority of men use drainage after this operation. After the anterior peritoneal flap is sewed to the anterior vaginal wall, an assistant removes the vaginal pack which was laid before the operation. A two-inch vaginal pack is placed through the abdominal wound into the stump of the vagina, and is cut on the free end so there may be two wicks for draining the parametrium. The outer third

of the vagina is closed in such cases, and, occasionally, the posterior vaginal wall is incised so that there may be an opening through which the serum may freely drain from the denuded areas. The two gauze wicks are laid loosely in the sides over the parametric denudation, taking care that they do not come in contact with the ureters. If they do, they may cause necrosis and subsequent fistulae. The peritoneum is now closed over the drains and the sigmoid sutured across to complete the separation of the abdominal and pelvic cavities. If drainage is used, it should remain *in situ* for five days, a short piece being removed daily after forty-eight hours. If the tampon is removed too

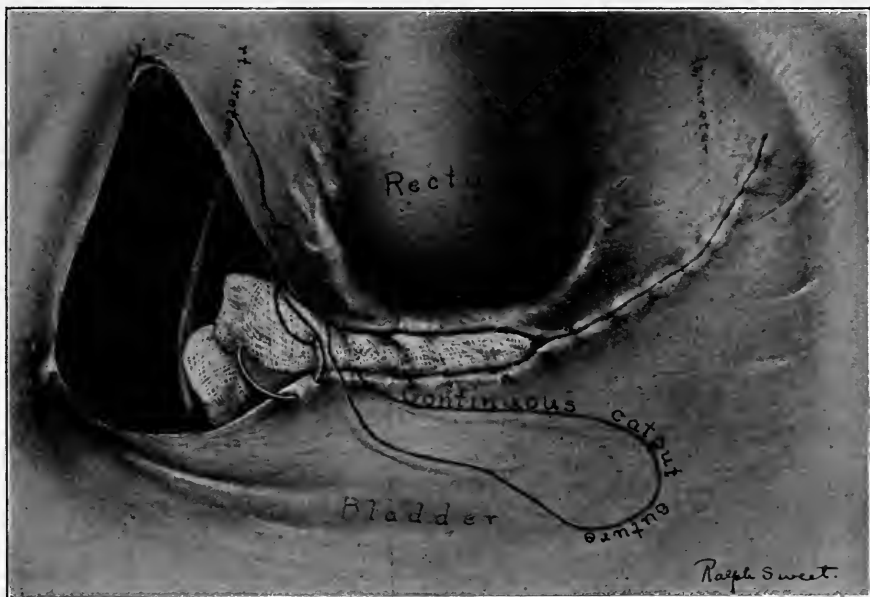


FIG. 66.—DRAINAGE AFTER REMOVAL OF UTERUS AND PARAMETRIUM. Gauze drain has been inserted into the vagina. The rectum and bladder have been attached to the posterior and anterior vaginal wall. Right half of figure shows peritonealization.

early, secondary hemorrhage may result from infection, and even a fatal issue may follow if secretions have been profuse and hemostasis was not good at operation.

Closing without Drainage.—The experience of Bumm is most helpful in connection with closure without drainage. It is Bumm's belief that the most careful and thorough peritonealization is of the greatest importance, and is responsible, together with closing without drainage, for the reduction of mortality which has occurred in his clinic. When the free surfaces of the wounds were drained with gauze into the vagina, there was 30 per cent mortality for 138 cases. In 35 per cent of the mortality, suppuration and necrosis occurred in the tamponed cavities from which there developed ascending peritonitis. Before he was willing completely to abandon drainage, he placed a small drain in

the lower angle of the pelvic peritoneum and carried it out through the vagina. During this period the mortality was reduced to 21 per cent, and deaths, for the most part, occurred from ascending peritonitis. He now closes all surfaces of peritoneum with a double row of sutures to insure their remaining in place, and uses no drainage. The mortality of his last 100 cases closed in this manner was but 6 per cent. Bumm believes that the tampons only excite a secretion from the wound, which forms an excellent media for the growth of pathogenic bacteria which are always present in the cancerous ulcers. If the peritoneum is carefully closed at all points, it can easily handle a considerable amount of virulent organisms.

After Treatment.—The after care and postoperative treatment is an important item in the ultimate result of the operation. The radical operation is often attended with shock, since it should require at least two hours for its completion. It is a safe rule that operations which last for a shorter time are not likely to be radical. Much saving in time can be effected only by omitting important features of the operation. Infusions of saline are often necessary upon the operating table, and the patient should be surrounded with hot-water bottles as the operation progresses. She should be placed in a thoroughly warm bed and given infusions. Shock may be combated by bandaging the legs or the injection of 10 to 20 minims of a 1 to 1000 adrenalin chlorid solution. We use Murphy drip as a routine, as soon as the patient is in bed after the return from operation. It is best given slowly—35 to 40 drops per minute. Cardiac dilatation should be met by camphorated oil and other heart stimulants. Pituitrin is useful in this connection. The bladder should be catheterized at intervals of five hours. Many use a retention catheter in all cases; yet this, in our judgment, has no advantage. Postoperative bronchitis and hypostatic pneumonia may cause troublesome complications. Their frequency is reduced by moving the patient frequently after operation. The bowels should be opened by a gentle catharsis on the third day after operation. Gas pains are often relieved by enemas any time after thirty-six hours following operation. Pituitrin is useful as an adjunct. When the patient is able to retain fluids, the Murphy drip should be discontinued. When nausea and vomiting are long maintained, they may be best treated by stopping all fluids by mouth or rectum and using only hypodermoclysis. Gastric lavage should be given on suspicion of gastric dilatation.

Complications.—The chief complications are from shock and infections of the urinary tract. Cystitis is nearly always a necessary evil, complicating radical operations for uterine cancer. Urotropin in 10-grain doses is advised for internal medication four times daily; yet we have seen few results from this routine comparable with those obtained from irrigations of the bladder twice daily, with a half saturated boric solution, leaving an ounce of 1 to 400 silver nitrate solution in the

bladder. Vesical fistulae are likely to arise spontaneously, especially in the cases which have been complicated by anterior adhesions. They generally close without difficulty. More serious are the bladder injuries, which occur near the ureteral insertion, caused while freeing the ureter. They usually present symptoms a few days after operation. They may be best treated by a retention catheter, which may be left in for a maximum of ten days. The operative result from the closure of these abrasions is often not good. The operation itself may be attended with great difficulty. The ureteral fistulae were formerly believed to heal spontaneously only in rare cases. By delaying active treatment many heal spontaneously. Weibel emphasizes the importance of expectant treatment for this complication, and advises the routine treatment with a caustic. Failing to secure closure, the majority of operators in this country attempt to insert the ureter into the bladder. Wertheim and his followers on the continent of Europe usually favor nephrectomy, unless the other kidney has been found diseased. Before resorting to this operation, the condition of the bladder, ureter and kidney should be determined by a cystoscopic examination. Thrombosis is not infrequent, and emphasizes the importance of handling carefully the big blood vessels in the pelvis. Peritonitis is the frequent cause of death, and always threatens with the presence of the infected cancerous ulcer.

Complications During Operation.—It is not always possible to determine the extent of bladder involvement before operation. The cystoscopic evidence of malignant invasion of the bladder has already been mentioned (page 199). Nor is it possible to determine the condition of the ureters prior to operation; yet it may be found nearly impossible to separate the bladder from the cervix or to free the ureters from the parametria because of fixation. When the latter occurs, there is usually a hydro-ureter above the point of fixation. Some have claimed that if the ureter cannot be freed without much trauma, it is better to resect the terminal part of the duct and implant it in the bladder. Sampson's experience does not bear this out, since he found that secondary infection of the kidney was so common as to constitute the rule, when the ureter was cut and transplanted by a careful method. The majority of men proceed with the operation, since they have usually lost the chance to withdraw when the operation has progressed to this point. The technic for ureteral transplantation is as follows: the upper end of the severed duct is grasped with two silk sutures for a guy; a clamp is passed into the bladder through the urethral orifice and an opening is made into the fundus of the bladder; the sutures, designed for use as guy ropes, are grasped and the ureter is pulled into the bladder for a distance of 1 or 2 centimeters. The ureter is then attached with a few stay sutures to the bladder wall, taking care that there is no tension on sutures in the wound. An exact peritoneal

covering completes the process. When the ureter is fairly short, the bladder may be freed and fixed to the iliac fossa, which will prevent tension on the sutures uniting the ureter in the bladder wall. If the ureter has been cut accidentally, a ureterostomy is done by implanting the upper end of the duct into a slit in the vesical end. If too much of the duct has been destroyed or cut away to permit any of these procedures, and it does not seem good judgment to attempt the removal of the kidney at the time, the upper end of the ureter may be tied off and the lower end of the duct freed from its supports, leaving the kidney to determine its own problem. Various things may happen in the latter event. Spontaneous atrophy may occur, as may pyelonephritis, which may require a subsequent extirpation. The rectum is often injured during the separation. Immediate repair is usually followed by good results. Occasionally rectal fistulae develop following tampon drainage. They also usually close spontaneously. Injuries to the deep blood vessels in the pelvis may readily occur during attempts to remove the lymphatic glands. Even the external iliac vein may be traumatized. There are reports, however, of its successful suture.

Mackenrodt's Operation.—The usual preparation of the vagina and abdomen are carried out. The patient is put in the high pelvic elevation. Mackenrodt advocates the employment of a horseshoe-shaped incision made as follows: the skin is put upon the stretch transversely and an incision is made down through the fascia of the recti muscles, the incision beginning about two inches above the symphysis and continuing laterally upward and outward to a point opposite the anterior superior spines; the fascia of the recti muscles are now split along the line corresponding to the skin incision. The muscles are separated in the midline, and divided transversely some 3 or 4 centimeters above their insertion. The peritoneum, together with the epigastric vessels, is now pressed downward, and the fascia connecting the recti and oblique muscles is divided parallel to the skin incision. The peritoneum is next divided above the bladder along the line of the skin incision, out to, but not through, the epigastric vessels. During this step great care must be made not to injure the bladder, which may be loosened from its attachments about the symphysis during the previous manipulations. If the upper edge of the organ is not visible, it can be palpated between two fingers. The convex upper flap with its peritoneal lining is now pressed backward and clamped to the peritoneum of the upper portion of the posterior pelvic wall, thus shutting off the abdomen from the pelvis after the intestines have been placed within the abdomen. The margins of the wound are now draped with sterile towels.

The peritoneal arca which is to be extirpated, is outlined by a line passing between the bladder and the uterus, laterally over the round and in-

fundibulopelvic ligaments along the posterior layer of the broad ligament at the pelvic wall, and mesially across the rectum at the level at which the peritoneum of the cul-de-sac becomes firmly fixed to the bowel. The uterus is elevated and drawn to one side, while the vesico-uterine fold peritoneum is incised. The round ligaments and the infundibulopelvic ligaments are tied on both sides. The rectum is freed from the posterior surface of the uterus and cervix with sharp and blunt dissection. When the peritoneal incision nears the rectum, great care must be taken not to injure the ureter, which often runs close to the bowel. The broad ligaments are opened up, and the connective tissues of the latter are separated from the pelvic wall. The connection between the cellular tissue and the pelvic wall is very loose, and can be separated without bleeding by stripping it down with gauze, even as far as the levator fascia and the origin of the uterine artery. This step is facilitated by using clamps as retractors attached to various portions of the broad ligaments. The blood vessels of the lateral aspect of the pelvic wall are now readily seen. The adjacent lymph glands are also exposed by this procedure.

The *ureters* are not freed or isolated until both broad ligaments have been opened up in this manner. The uterus and parametrium will hang suspended only by the base of the broad ligament, bladder, and vagina. The uterine arteries are ligated near their point of origin. It is best to cut them between ligatures to prevent reflex bleeding. The fibers of the parametrium are now separated and the ureter is removed from its sheath in the manner previously described. Between the ureter and the uterine arteries is a lymph gland which is nearly always the seat of carcinomatous involvement. Before the ureter can be completely freed, the bladder must be separated as described in the former operation. The same procedure is done on the opposite side. The greatest care should be taken to avoid unnecessary ligatures on the bladder, since they constitute a menace to the integrity of the organ.

Now follow the most important steps of the operation, namely the *separation* of the roots of the *parametrium* and of the *paracolpium*. These two structures are anatomically continuous, and are composed of the same type of tissue. Mackenrodt emphasizes the importance of dissecting them cleanly from the floor and sides of the pelvis, since he claims that ligation and division of these structures favor recurrences. The lower external portion of the pelvic parametrium consists of connective tissue bands which diverge in all directions, corresponding to the distribution of the lymph and blood vessels, and merge with the sacral pelvic fascia, the obturator fascia, the rectum, and the peritoneum of the cul-de-sac.

There are three groups of veins which must be controlled to prevent loss of blood and avoid the prolongation of the operation. These are: (a) the anterior division of the parametric veins which empty into the obturator vein and anastomose with a vaginalvesical venous plexus; (b) the middle division which empties into the hypogastric vein; and

(c) the posterior division which drains the posterior parametrium and communicates with the sacral, hemorrhoidal, and with the veins on the rectum. The obturator nerve runs between the hypogastric roots and the pelvic parametrium, and about it are the lymph glands of the hypogastric group. The lymphatics follow the course of the anterior division of the veins to the internal inguinal lymph nodes. Around the middle group are lymph tracts which empty into the hypogastric glands. In the posterior upper division are lymphatics which extend to the sacral and prevertebral lymph glands of the lumbar vertebrae. The largest lymphatics accompany the uterine vessels and, for the most part, empty into the iliac lymph glands. Those from the ureteral glands also follow the same course; less often they empty into the glands which are located at the bifurcation of the aorta. The iliac glands also receive lymphatics which accompany the anterior group of veins from the inguinal region.

The vaginal pack is now removed and the uterus is drawn upward so as to put the vagina on the stretch. The anterior vaginal wall is then divided at the level at which the ureters enter the bladder. Before the incision is continued posteriorly, the rectum is pushed downward and freed. The vaginal edges are now supported with clamps which constitute a good means of traction while the uterus is removed. The vaginal cuff is now closed. The rectum can now be freed without difficulty, and the connective tissue bands of the paracolpium, which extend from the rectum to the sacrum, can also be separated from the bone by pressure with gauze. The connective tissue bands which extend from the vagina to the sides of the pelvis will require more careful attention, since they contain veins which anastomose with the vesicovaginal plexus, and the obturator veins which, if injured, may give rise to troublesome venous hemorrhage. Consequently, they must be exposed and ligated carefully, without injury to the obturator artery, after which the connective tissue bands are stripped off with gauze on the finger or on a clamp. There are also, in this middle root of paracolpium, one or two veins which empty into the hypogastric vein, which should be ligated before the tissues are removed. When the sides of the anterior portion of the paracolpium are freed, the whole mass of deeper pelvic connective tissue and vagina will be held only by the fascial insertions on the anterior sides of the pelvic cavity. These may readily be severed with scissors. The connective tissue mass comes away under traction in long bands which contain lymphatics of the rectal and sacral regions. The tissues thus removed, consisting of vagina, uterus, adnexa, and the shaggy connective tissue of the parametrium and paracolpium, form quite a bulky mass. Hemorrhage is now controlled and any further lymph glands that are present may be removed. These are found to consist of the obturator, inguinal, and iliac glands. If the connective tissue has not been

thoroughly removed, many of the glands may be overlooked as they lie in masses close about the vessels. He now drains to the vagina from the raw surfaces in the pelvis, and is most careful to prevent the drain from coming in contact with the ureters. The peritoneal layers are closed over the pack, the rectum being united to the vesical flap. The abdominal wound is closed in layers, the muscle and fascia being united by wires.

Complications.—The fatalities have come chiefly from albuminuria and nephritis. These complications have occurred 20 times in 70 cases, 8 of them with fatal result. Necrosis of the bladder occurred 22 times, due, he believed, to involvement of the bladder wall either with carcinoma or inflammatory processes. In 15 cases the bladder was fixed so firmly to the uterus that its separation resulted in an injury to the wall. Carcinoma was found in the bladder wall in 10 cases, and in the connective tissue between the bladder and uterus in 4 cases. He enucleated the ureter in 48 cases from an infiltrated broad ligament. There was necrosis in 3 cases. The ureters had to be excised in 3 cases, since they could not be separated, and the free upper ends were then transplanted into the bladder. Only one of these cases resulted successfully, death following one, and a fistula into the rectum in the other. The ureters were incised accidentally during two operations in cases in which they lay in the fold of Douglas and were cut through in the first stages of the operation. Transplantation was performed in both cases with resulting death in one and recovery in the other. The after care does not vary from the preceding operation.

Bumm's Operation.—Bumm believes that the success of a radical removal of a carcinomatous cervix depends upon exposure of the so-called vascular areas in the depths of the pelvis. He ligates the ovarian vessels on both sides, opens up the peritoneum from the insertion of the mesosigmoid on the left and the mesocecum on the right, clamps and cuts the round ligament, and continues his incision to the attachment of the bladder and cervix. On separating the broad ligaments from the lateral pelvic walls, the iliac vessels and the ureters are easily brought to view. In the upper portion of the exposed area is seen the common iliac vessels at the point of their division. When the posterior layer of the broad ligament, to which the ureter is fastened, is drawn toward the median line the origin of the uterine artery is exposed, as are the lymph glands in these so-called vascular areas. The ureter and the vessels are now freed, and the lymph glands in the vascular triangle are loosened at the same time. All small vascular branches must be ligated, or they will tear and bleed. When the lymph glands with the adjacent fatty and connective tissue are freed, the branchings of the common iliac, external iliac, and hypogastric arteries, and the accompanying veins lie exposed as if by dissection. The ureter is drawn to one side and the uterine artery is now doubly ligated and

divided. The entire vascular cord with the surrounding structures of fatty tissue, lymph vessels and glands are drawn to the midline. The ureter, which has been exposed only to the point just above where it is crossed by the uterine artery, is freed by blunt dissection as far as the bladder. This separation must be complete, since all the underlying tissue must later be removed. The uterine veins must be ligated before the ureter can readily be freed. There are two of these, the larger as big as the quill of a goose's feather, runs beneath the ureter, while the smaller lies above it together with the artery.

The remaining steps of the operation include the removal of the cervix, upper part of the vagina, paracervical and paravaginal tissue. Bumm agrees with Wertheim that the removal of the parametrium and paracolpium is much more important than the ablation of the lymph glands. The excision should be carried out as far as possible, even to the pelvic walls and down to the pelvic diaphragm. He closes the vaginal stump and unites to it the serous surfaces of rectum and bladder. As has already been stated, he does not employ drainage.

The Paravaginal Operation.—Schuchard, in 1893, advocated deep lateral incisions in the vagina to obtain wide exposure of the vaginal vault, cervix, and parametrium. This incision, therefore, facilitates a wide removal of pelvic connective tissue by the vaginal route. The paravaginal operation was developed by Schauta, and was built upon this exposure (Fig. 58). For fear of implantation of cancerous material in the wound, Schauta recommended that it be made as late as possible. Schauta's operation carefully dissects and exposes the ureters, ligates the uterine arteries well out to the walls, removes an enormous cuff of parametric tissue, as well as a large portion of the vaginal wall. He emphasized the fact that the radical vaginal operation is in no way akin to the simple vaginal hysterectomy.

The operation is performed in the following manner: after the patient has been shaved and the parts carefully prepared, she is placed on the end of the table in the lithotomy position. A speculum is introduced and the condition of the growth inspected. The vagina is now cleansed, the speculum reintroduced, and the cancerous ulcer is thoroughly cauterized with soldering irons as cauteries. The vulva and vagina are now again disinfected and the cervix is steadied with a tenaculum. A circular incision is made in the upper vagina below the growth after putting the vaginal walls on tension with tenacula and cutting between. In the early cases the incision should be made at about the junction of the middle and upper thirds of the vagina. In the later growths, it should be located so that half of the vagina can be removed. Many prefer the cautery instead of the knife. The vaginal cuff is now dissected off as deeply as possible and sutured over the cancerous cervix, so that infectious material may not escape from the uterus during the operation and contaminate the field. Tena-

cula or guy sutures are placed through the cuff for use as tractors, and to afford landmarks of the cervical position. There is some hemorrhage which results during this step which may be controlled with fine ties. A wide dissection is indicated, because of the frequency of cancerous extensions in the vagina not visible to the naked eye. Schauta insisted that the bladder be separated from its attachments before the paravaginal incision is made, since the latter step is useless if it is found necessary later to abandon the operation. The bladder is dissected first into the midline and later in the sides which can be best accomplished by dissection with the blunt scissors. The ureters lie under the lateral supports of the bladder, and are not exposed until the next step of the operation, when the parametrium is freed. If it is necessary on account of the extent of the growth to resect either the ureter or the bladder, the operation should be abandoned at this point before the peritoneal membrane has been incised. The paravaginal incision is now made. It is, in effect, only a wide episiotomy. The incision on one side usually suffices, and is best made on the side of the greatest parametric induration. Some, as Staude, recommend that it be made on both sides as a routine procedure. Other things being equal, the left-sided incision proves more convenient for a right-handed operator. The posterior portion of the left labia is seized with the forefinger and thumb of the left hand while an assistant puts the upper part of the labia upon the stretch. The incision is made from the posterior margin of the circular incision in the vagina, downward and laterally, through the posterior portion of the labia minus to the middle of the coccygeal region. The whole vaginal tube is incised in this manner. Schuchardt states that the cut passes through the left labium minus, the paravaginal and pararectal tissues, the levator ani and coccygeal muscles, the cellular tissue of the ischiorectal fossa, the skin of the perineum and the left anal region down as far as the rectum. The incision in the pararectal tissue is carried only far enough to the left, so that the rectum and sphincter ani may not be injured. A finger's breadth from the midline is usually sufficient. There is copious hemorrhage which cannot be entirely checked by tying off bleeding points. It may, however, be perfectly controlled by packing gauze into the wound and resting the weighted hanging speculum upon the pack. The effect of the incision is quite remarkable. The vagina now appears only as a shallow excavation, not more than an inch in depth, and at the bottom of it lies the parametria in full view.

The next step is the *separation of the ureters*. It is not necessary to catheterize them so that they will be better landmarks. The dissection is made under sight with the ureter in full view. Experience has shown that the ureters are more likely to become infected if there has been preliminary catheterization. The dissection of the bladder is now continued laterally, and at the level of the internal os and under the lateral

attachment of the bladder, the ureter is found winding around the uterine artery. Unless the infiltration is quite marked, the ureter can be freed readily from its bed. The uterine vessels are ligated as far away from the uterus as possible. They should be tied as soon as the landmarks are established so as to check the bleeding. The pouch of Douglas is opened and the incision is carried well out on the sides of the pelvis. The parametrium is separated from the rectum by blunt dissection, during which step a branch of the middle hemorrhoidal artery is encountered and must be tied. Schauta claimed that if this vessel is tied, and if the uterine artery has been ligated high up as a preliminary step, only venous oozing will result while the parametrium is hooked down over the finger and is cut free with scissors. The ureter should be constantly in view during this step so that it may not be injured. Other operators have advised ligation of the parametrium before it is cut away. Yet no one who ever saw Schauta perform this operation will believe that this is necessary. It is astonishing how easily an infiltrated parametrium can be removed even from the pelvic wall. If the anterior peritoneal cavity has not been opened, this is now done when the uterus will hang suspended only by the tops of the broad ligament. The bladder and ureters are elevated, the fundus of the uterus is seized and pulled down while at the same time the cervix is pushed up into the wound. The ovaries are then brought into view and their vessels are tied, when the tops of the broad ligaments are cut away between clamps, or after hemorrhage has been arrested by pedicles. Schauta did not remove the tubes and ovaries, claiming that they are practically never the seat of cancerous extension, a claim which we do not believe is worth making if the operation is designed to be radical. The stumps of the ligaments are brought down into the wound and the peritoneum covering the bladder is united to that on the side of the rectum. All raw surfaces are made extraperitoneal. The vagina may be drained or not, depending on the judgment of the operator. Schauta, Schuchardt, Gellhorn, and others who have used this operation have employed drains, yet we believe the experience of Bumm with drainage applies equally well to the same condition and that drains should not be employed if hemostasis has been effected. The paravaginal incision is closed with catgut carefully approximating all tissues. Retention sutures should be used to reinforce the closure.

The after care is the same as that of any serious abdominal operation, namely, to prevent shock and to provide for eliminations. Post-operative cystitis is common and infection of the paravaginal incision has been often noted. There have been cases where carcinomatous elements have been transplanted into the incision. If packing has been employed as pelvic tampons, its removal should begin two or three

days after the operation, withdrawing an inch or two of packing each day so that the entire drain is out at the end of a week.

The method is not free from *accidental injuries*, even in Schauta's hands, since it is a serious undertaking, although the primary mortality is somewhat below that met with after the abdominal operation. The convalescence was uninterrupted in 150 of Schauta's series of 258 cases. Postoperative cystitis occurred 67 times and the bladder and ureters were injured each 11 times. The intestines were injured 4 times. The paravaginal incision broke down completely in 5 cases and there were 2 cases in which carcinomatous tissues were grafted into the wound. Yet this type of operation is particularly favorable for stout women in whom abdominal exposure is gained only with the utmost difficulty.

OTHER OPERATIONS FOR CANCER OF THE CERVIX

The Cautery Methods.—The cautery is doubtless the oldest method of treatment for carcinoma of the cervix. The methods have been revived from time to time. Especially have the remarkable results obtained by Byrne redirected the attention of American surgeons to the possibility of satisfactory treatment by cautery amputations. Byrne began his work in 1872, and during the next dozen years operated on 367 cases without mortality. His method for the most part consisted in the amputation of the cervix by means of a cautery knife. This was followed by burning out the interior of the uterus by similar instruments. He claimed cures of 19 per cent for cases under observation for five years. His results were much questioned by surgeons throughout the country, yet practically all who knew first hand of his work have remained more or less enthusiastic about it. Rawlick, Moore, Madden, Dickinson, and others revived the method which, however, did not obtain wide vogue throughout the country. All who have used the cautery, instead of the knife, claim that the influence of heat extends beyond the actual field of operation, which permits a more radical operation than it would seem at the time possible. Bumm, among others, denies this and believes that the effect of the cautery does not extend more than 1 centimeter into the tissue. Certain it is that the burning done by a Paquelin cautery on a piece of raw meat does not extend far from the margin of the scar, as can be proved readily by any one who will try the simple experiment.

Following Byrne, Werder became converted to the cautery treatment of uterine cancers and has remained so enthusiastic that he abandoned the radical operation proposed and practiced by him, which is identical in principles with the method later advanced by Wertheim. The operation first employed was a more radical type of the method practiced by Byrne. It was in effect a vaginal hysterectomy, in which

he used the Schuchardt paravaginal incision in cases which did not permit of good exposure. Subsequently he used a combined vaginal and abdominal operation, because he found that the ureters were not readily protected from injury by the heated clamps in the vaginal hysterectomy.

Werder's Cautery Hysterectomy.—The vagina was cleaned with antiseptic preparations after the patient had been shaved and prepared. The patient was brought to the edge of the table, the cervix exposed by a hanging speculum, and steadied by a tenaculum. An incision was then made about the vaginal fornix, as far as possible from the affected area, by means of a cautery knife developed by him and kept at dull heat to prevent burning through the blood vessels without first sealing them to obtain hemostasis. Werder insisted that the proper degree of heat could be obtained only when the cautery knife was placed against the tissues before the heat had been turned on. Traction was made upon the cervix and, as the base of the parametrium was charred through, new areas were exposed. The dissection in this manner was carried through the base of the broad ligaments and around the entire lower uterine segment until the peritoneum was reached, care being taken to keep the bladder and bowel from the neighborhood of the hot knife. The peritoneum was then opened posteriorly by scissors and the opening widened by the fingers, when the wound was carefully inspected to see that all the surfaces were black and well charred. A vaginal pack was now laid and the patient prepared for a laparotomy.

A midline incision was made, and the field prepared for operation by packing back the intestines into the abdominal cavity by wet saline gauze. The peritoneum of the bladder was incised from side to side, cutting into the vagina. The infundibulopelvic and round ligaments were then burned through with a broad Downe's electrothermic clamp until the tissues were well charred and there was no bleeding. Later, Werder used ligatures for these structures, because cancer practically never attacked them. The greatest care was taken that the treated parts were properly exposed, so that adjacent structures could not be injured by the heat. The broad ligament was then treated in a similar manner, starting on the least affected side. Werder worked with comparatively small bits of tissue, thoroughly charring each one before dropping the stump. He cautioned against dropping a vessel until it had been observed for at least one minute after it had been burned through. If the directions were followed, hemostasis was as secure as that resulting from ligatures. The opposite parametrium was then treated in the same way and the uterus removed by pushing it down through the vagina or occasionally by removing it through a carefully walled-off field. He took the greatest care to avoid injury to the ureters. After the removal of the uterus, the vaginal stumps were

exposed and the cauterized edges turned downward, following which the raw surfaces were approximated with catgut sutures. The peritoneal surfaces from the bladder and the rectum were then covered with peritoneum, and all other raw surfaces in the pelvis were covered to secure a smooth peritoneal floor. The abdomen was then closed.

It will be seen that this operation differs from the ordinary hysterectomy which has been performed through the vagina and abdomen only in that the cautery is used instead of the knife, and that there are few, if any, ligatures needed to secure hemostasis. The ureters were protected from injury by pulling the uterus to one side. Consequently there is no removal of the parametria. The pelvic glands were not attacked. In 1913, Werder reported his results. The primary mortality was but 5.1 per cent. He states that 46 per cent of his cases which had been under observation for five years were cured. Four of these, however, succumbed later to cancer. His results are treated separately under the general heading of results following operation (page 225).

Vaginal Hysterectomy.—Probably, at the present time, the great majority of cases of cancer of the cervix in America which have been operated have been treated by vaginal hysterectomy. Few believe that it is in any sense curative, although it has been taken up again by a number of men who have felt that the primary mortality of the radical operation was more than they could endure. These practically without exception confess their inability to cope with the cancer situation, and perform simple vaginal hysterectomy with the idea that it is a palliative measure, and may cure an occasional case where the disease remains limited to the uterus. Personally we have never seen a case which was cured by vaginal hysterectomy. We also have had a very unusual opportunity to judge of the results of others who have treated cancer of the cervix in this manner. During the last few years, we have seen a large series of cases where recurrence was almost immediate after this operation, the patients being sent to our clinic for postoperative radium treatment. For this reason, the method will not be described. Van Ott alone recommends the method as a proper measure. His statistics are given on page 261.

High Cervical Amputation.—This operation was formerly performed with the idea that it might be radical. Very rarely, it was followed by a reported cure. It has been entirely superseded by the radical operation. It should not be done under any circumstances (Fig. 67).

PALLIATIVE TREATMENT OF CANCER OF THE UTERINE CERVIX

The palliative treatment is entitled to serious consideration, because the vast majority of cases in America first present in an inoperable

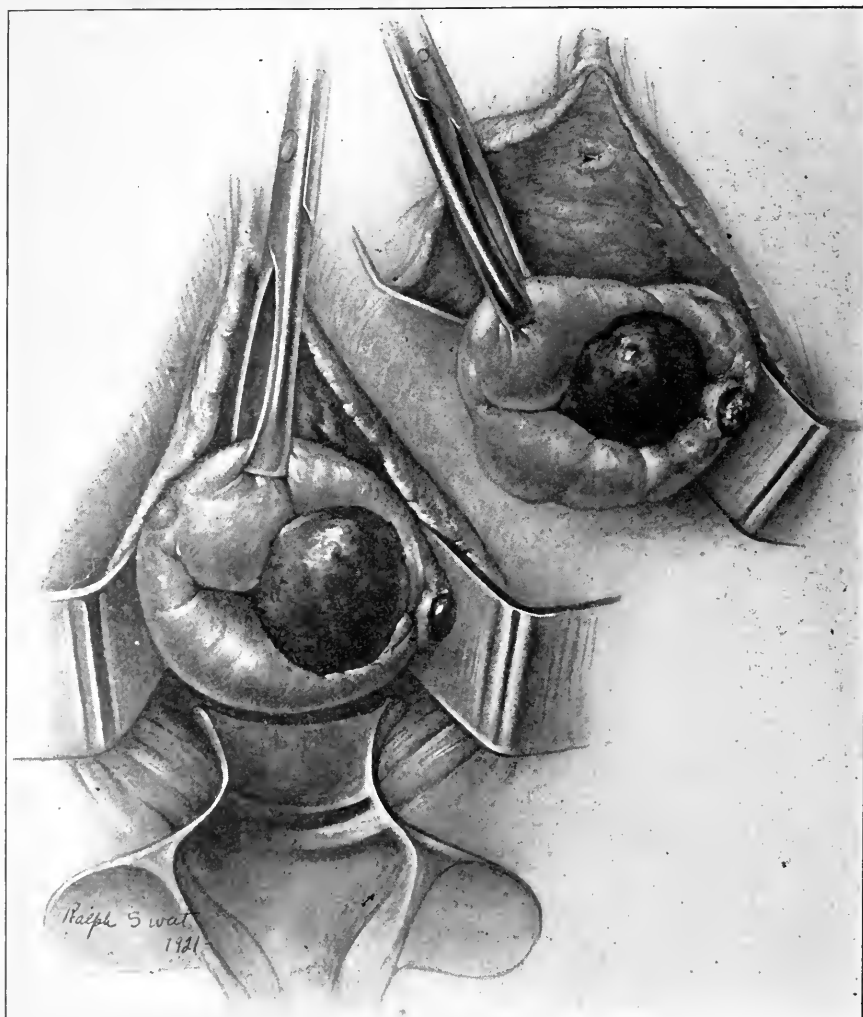


FIG. 67.—RECURRENT OF CANCER TEN WEEKS AFTER CERVICAL AMPUTATION.

condition. There is no doubt that much can be done by comparatively simple measures to alleviate the pain, control the offensive odor of the disease, and occasionally to retard the development of the growth.

Medical literature is fairly teeming with the reports of various methods which have been tried, and practically without exception have

been superseded by others which in turn enjoyed temporary vogue. They come under various classes. Some aim to treat as general methods acting through the body system, others have been designed to act as local measures.

General Methods.—These have aimed to control cancer by modifications in the diet, by administration of drugs, or by introducing antibodies in the form of ferments, serum, etc. Some have recommended a vegetarian diet, others a two-meal system, while the purin-free diet had some basis from the experimental standpoint.

Various drugs have been used in all types of medication by mouth, by the rectum, under the skin, and into the veins. Arsenic has been used in the form of Fowler's solution, and in sodium cacodylate. Mercury and quinin, decoctions of cinnamon, of violet leaves, alder leaves, infusions of nettle condurango, chelidonium-majus, charcoal, cholestrin, jequirity, all have had their advocates. Oleate of soda, cinna-mate of soda, orthocoumarate of soda, have been given hyperdermically as has salvarsan. Eosin-selenium was developed by Wassermann, yet has proved unsatisfactory. Nearly all the glands of internal secretion have been exploited without definite results. Trypsin, cholin, and other ferments have enjoyed considerable vogue but have been found useless.

Various caustics have been employed for local treatment, usually after curetting. Sometimes they have been injected into the body of the tumor. Among this list we may mention fuming nitric acid, bromin in alcohol, nitrate of silver, methyl blue, acetic acid, formalin, arsenic pastes.

In 1884, A. Reeves Jackson introduced tampons of zinc chlorid after preliminary curettage. Czerny revived the treatment. After rather extensive curettage, a tampon of gauze saturated with 30 to 50 per cent solution of zinc chlorid is packed into the ulcer. It is allowed to remain in place for three days, after which it is withdrawn and douches are given. Some, as Buttersack, have questioned the efficacy of the treatment, claiming that any chemical used as a caustic is quite beyond the control of the physician. Yet the method is popular, and many believe it has a selective action upon the cancer cells, and does much to clean up the ulcer.

Acetone Treatment.—Gellhorn, in 1907, introduced acetone to clean up the ulcer. His method is as follows: the patient is anesthetized and all sloughing tissues are removed with a curette. The crater is gently dried with cotton pledgets. The vagina and vulva are then thickly smeared with vaselin so that the acetone may not come in contact with skin surfaces. One ounce of acetone is now poured through a tubular speculum into the crater of the cancer, and is allowed to remain in contact for twenty or thirty minutes. The excess of acetone is now removed, and a gauze strip saturated with acetone is packed into the

ulcer and held in place for several hours. Subsequent treatments are required two or three times weekly. They may be conducted at home or in the physician's office, since an anesthetic is not required. The hips are elevated and the speculum is filled with acetone. Gellhorn states that the patient may hold the speculum in place so that the acetone remains within the vagina and does not run over the skin surfaces. If it does come in contact with the skin or rectum, it turns the tissues white, and produces a disagreeable sensation of burning. This may be checked by an application of cold water. After the treatment of a half hour, the vagina is dried, and a cotton tampon is introduced in the vagina to hold the walls apart. It is removed in a few hours. The hygroscopic qualities of acetone cause the tissues to shrink rapidly and thus causes contraction of small bleeding vessels. Oozing is quickly checked by the treatment, and the bleeding surfaces are converted into whitish films. There is considerable contraction of the ulcer after a few treatments. There should be no pain resulting from the method. We have had much success from the method, which we used considerably before becoming interested in radium. We used it after cauterization and did not curette as a preliminary treatment.

Cauterization.—Cauterization in many instances has brought about marked improvement in the general condition of the patient through its effects in cleaning up the cancerous ulcer. Occasionally, with the disappearance of the septic necrotic material in the ulcer, there has been improvement in the feeling of the broad ligaments which have been considerably softened. Lomer has stated that cauterization has occasionally caused temporary arrest of the growth. There are many instances in which the recurrence of the disease has had a prolonged latent period, after an incomplete removal by operation, as a result of the cautery method. Freund even advocated removal of the uterus in such cases which appeared to have improved after cauterization, claiming that even the hopeless cases were given temporary relief. Our experience does not support this view, and we feel that modern investigation shows that it is bad surgical judgment. The advent of radium into the therapeutic field obviates the necessity for any operations which cannot be radical.

The Percy Method of Cauterization.—Percy developed the method of cauterization by using large irons and comparatively low heat. He makes a great point of the fact that he does not apply heat of sufficient degree to burn the normal tissues, but merely to make the cancerous mass so hot that the cancer cells are killed. There is some experimental basis for the view that cancer cells are not as resistant to heat as are normal tissues. He insists upon avoiding actual chars, since they inhibit the further dissemination of heat through the cancerous tissues, and also prevent drainage. He states that charring the surfaces also permits a greater absorption of broken-down cancer cells

which may react unfavorably upon the body system. His method was taken up most extensively and has had a sufficient trial so that we may judge of its results. Many claimed that radical operations could be performed on cases which had been considered inoperable before the application of heat. The Mayos operated a series of this type of cases, as did Clark of New Orleans. The authors believe that the favorable results following the Percy treatment were more apparent than real, and the softening of the parametrium followed the cleaning up of the infected ulcer rather than from controlling the cancer. That is to say, that the actual extension of the cancer in these favorable cases was probably not as great as seemed indicated by the findings at the time of the first examination.

In his early cases, Percy merely burned the cervical growth with a large electrically heated iron. He emphasized the fact that the curette should never be used in the treatment. Later, he advocated opening the abdomen and ligating the internal iliac arteries, not only to cut off the circulation and thus starve the malignant tissues, but also to prevent the sloughing and hemorrhage which may follow extensive cauterization. He believed also that the treatment could be better directed if the uterus were held in a gloved hand while the cautery was applied. Percy developed water-cooled speculum to prevent burning of the normal tissues of the vagina. He advocated burning the cancer until the fundus of the uterus is too hot for the assistant to hold in his hand encased in a medium weight of a rubber glove. The treatment requires at least two hours under anesthesia. He states that about 50 per cent of the cases may need a reapplication of heat. He claims that secondary radical operations should not be performed, even if the case later seems to be operable, since nature has developed an immunity which may be broken down by the operative interference. He believed that his technic was applicable to 95 per cent of women with good kidneys and a fair heart, suffering from inoperable carcinoma with the expectation of arresting the discharge, checking the hemorrhage, inhibiting the septic absorption and improving the general nutrition of the patient. In a smaller group of cases, comprising about 35 per cent of inoperable uterine carcinoma, he states that you may expect occasional cures if there are no metastases outside the pelvis. He reports 65 cases in this group, 4 of which have survived more than five years. Of these, one lived nine, one six and a half, and two five years. While Percy mentions other cases in this group which he states are clinically free from cancer from two to five years, we must disregard them from the standpoint of cure, although they are of the greatest interest, since they first presented as inoperable cases.

The method is not attended with uniformly good results. Fistula may develop in the bladder or rectum. Several cases have been reported where death followed from the burn. The method is not ideal

theoretically, since laparotomy is necessary as well as an operation which may last from two to two and a half hours merely for palliative purposes. Before the advent of radium, the method accomplished much, but in our judgment it has now been superseded entirely by radium.

The report of Bailey in 1922, suggests that the Percy method should not be combined with radium treatment. Bailey and Quimby, writing in 1922, say:

"During the year 1915-1916 a Percy or modified Percy operation was performed in thirty cases. The abdomen was opened and in all instances, the burning was conducted with an assistant's hand holding the uterus. In a considerable number of cases, the vessels were tied off in addition. The operation was followed by radium, the first application usually about two weeks after the operation. The results from this procedure were not good, the majority of the cases developing rectovaginal fistulae. However, there are three cases that have remained well up to the present (May, 1921). In one or two patients the results following the ligature of the vessels were disastrous, leading to a sloughing of the tissues of the pelvis.

"The criticism of this work would lead to the conclusion that the blood supply should not be interfered with to the extent of tying off the vessels and further that with the abdomen open and the uterus held in the hands of an assistant, there is a tendency on the part of the operator to burn too extensively and beyond what is advisable, if radium is to be used later. In other words, the tissue sloughed away following the burning leaves a very thin wall between the cervix and adjoining parts and the slough which regularly follows radium dosage, applicable to the treatment of cancer, breaks through this thin barrier."

METHOD OF CALCULATING RESULTS

There has been the greatest difficulty in the past in determining the actual results of operative treatment. Little was gained by comparing the results of different surgeons, since there was usually no agreement as to terms and consequently no basis for comparison. Some men operated only the most favorable type of cases, and claimed high percentage of cures. Others also attempted more advanced growths and presented statistics which suffered by comparison, even though they may have cured a larger percentage of the total number of cases applying for treatment. The majority of these series grouped together all cancers of the uterus, making no attempt properly to classify them. Naturally, therefore, the results would differ, depending on the selection of cases for operation and upon the relative pro-

portion of cervical and fundal cancers in the series, since adenocarcinoma of the uterine body is much more easily cured than are cancers of the cervix.

The older literature has proved conclusively that, in order to permit of comparisons of the various types of operative procedures, there must be complete agreement as to terms. Yet even with agreement as to definitions, and with cases properly arranged for study, there will be factors which we cannot control. There are variations in the malignancies of tumors of similar morphology and histology. The character of material may also vary in different years, even in the same clinics. These features, however, cannot be estimated and will be evened up only by the series running for many years. Due to the tremendous educational movement which has been made in Germany, more early cases now apply there for treatment. No one who has seen at first hand the works in cancers both in Europe and America can fail to be impressed with this fact.

At the present time, the majority of students agree that the ultimate cure of the disease should be expressed in terms of operative cures as well as the total number of cases applying for treatment. Men were urged to present their results in terms of absolute cures in order to prevent exclusion of cases. Absolute cures are no longer of the greatest importance, since radium has come into the therapeutic field. Properly presented, operative cures will completely express the result of the treatment. In making his report, the surgeon should present a complete résumé of his entire material, arranged in such a manner as to show: (1) the number of cancerous patients who sought relief during the series, classified as cancer of the cervix and cancer of the uterine body; (2) the number who were operated; (3) the number who were operable but who refused operation; (4) the number who were inoperable; (5) the number of those who died from the operation; (6) the number who could be accurately followed; (7) the number who were lost for purposes of study; (8) the number who died of intercurrent disease during the five-year period of observation; (9) the number in whom a recurrence was observed during this interval; and (10) the number who were free from recurrence at the end of a five-year period of observation.

Werner, Waldstein and Winter have been especially active in their efforts to develop methods which will permit of the comparison of cancer series treated by the various types of operations. They all agree that in our final computation we should omit from consideration cases which were operable, but which did not submit to the proposed treatment. There has been considerable discussion as to what constitutes operability. Some, in order to prevent improper exclusion of cases, would class any case as operable in which the operation was attempted irrespective of whether it could be carried out to the end.

Others believe that the surgeon should have the right to decide at the conclusion of the operation whether the removal was or was not entitled to be considered radical. It probably makes little difference so long as the cases are tabulated according as the operation was completed, or was tried but was abandoned because the local conditions prevented the proper completion of the operation. The majority of German clinics agreed with Winter, in 1908, that all cases in which operation was attempted should be considered as operable unless the local conditions prevented the radical operation from being carried out to the end. Wertheim, however, in order to avoid the appearance of exclusion of cases counted as radical all the operations that were attempted and completed, even with restricted resections.

The primary deaths may be excluded in calculating the operative cure on the ground that cancer kills unless cured by operation, although some do not feel that this is permissible. They must, however, be included in determining the absolute cure, which is the proportion the cases remaining cured for five years bear to the total number of cases who were willing to accept treatment, irrespective of their condition, that is, both inoperable and operable.

Cases which were lost track of during the period of study are excluded from the calculation of after results unless they had developed recurrence when last seen. This seems perfectly reasonable, although it is apparent that the value of a report may be greatly impaired by the necessity for excluding any considerable number of cases on this ground.

There has been much discussion as to how we should consider and classify the cases which died of intercurrent disease before the expiration of the five-year period of observation. Werner held that they may be regarded as cured if they live two or more years after the operation, provided recurrences could not be demonstrated in the scars or lymph glands by microscopic serial sections at a post-mortem examination conducted by a skillful pathologist. He claimed that they should be classed as recurrences if they died before two years, even if cancer could not be demonstrated. The heads of the German University clinics agreed with Winter, in 1908, that the intercurrent deaths should be excluded from the series unless there was evidence of recurrence.

The five-year limit is now generally accepted as the time at which freedom from recurrence should be regarded as an operative cure. It does not follow, however, that cancer may not cause death later. Yet the number of cases presenting recurrences after this time are so few that they more than offset the difficulty of following cases for a longer period. It is of interest that the majority of recurrences during this interval are local rather than regional, and that recurrences presenting later than five years are very likely to be in the regional lymph glands.

The literature shows that only a very small percentage of recurrence develop after five years. Winter, in 1908, states that in his series of 350 cases, there were only two which certainly, and two which possibly, presented recurrences later than five years after operation, and that the literature shows that not more than 10 of 1,000 recurrences are first observed after this period. Others think that the percentage is greater. Seitz found that 3 per cent of the recurrences from operation in von Winckel's clinic occurred in the fifth year. Wertheim, in a series of his first 250 cases which had been operated for five or more years, found 78 recurrences. Of these, 41 developed the first year; 24 in the second; 6 in the third year; 4 in the fourth; and 3 in the fifth year. Werder believes that late recurrences are more frequent than are generally supposed. In his series of 87 cancers operated by his cautery method, 8 developed recurrences between five and nine years after operation. Weibel, in 1914, stated that 13, or 7.7 per cent of Wertheim's 169 cases which had stood for at least six years had carcinoma again from six to eight years after operation. One other case developed a sarcoma of the foot. Among the 13 cases which again presented carcinoma, 1 was of the duodenum, 1 of the breast, and 1 of the clitoris. The microscopic picture of these tumors was so different from that of the original tumor that they were not thought to be recurrences. The remaining 10 cases (6 per cent) were undoubted recurrences in the pelvis. Of the total number of 13 cases, 6 developed in the sixth year; 5 in the seventh year; and 2 between seven and eight years. Weibel states that Wertheim's records show that there is about the same proportion of recurrences for each year after the third. Ries, also, observed the recurrence nine years after operation, yet, as has been stated, the practical difficulty of keeping cases under observation for more than five years more than outweighs the objection that recurrences may develop later, since statistics in which a considerable number of cases are lost sight of during post-operative observation are not of great value.

RESULTS OF RADICAL OPERATION FOR CARCINOMA OF UTERINE CERVIX

Although it is twenty-six years since Ries emphasized the importance of the resection of the iliac glands, together with the parametria, and twenty-three years since the advent of Wertheim into the field, there are unfortunately no large series showing the results of radical operation with the exception of Wertheim's. As we have elsewhere indicated, it is not easy to present results in form which permit of comparison with those of others. A good result should mean more than prolongation of life alone. The observations of Clark, that the

distressing sequelae of operation which may make life a burden should be recorded together with the results of the operation, have remained unnoticed.

Weibel, in 1913, reports the results of Wertheim's cases. During the years 1898 to 1912, there were 1,430 cases of cervical cancer in his clinic. Of these, 71 refused operation; 684 were inoperable. A radical abdominal operation was done on 675 cases, thus equaling a 50 per cent operability. The operability was gradually raised during the series: from 42 per cent in the first 250 cases, to 52 per cent between 300 and 500 cases, to 55 per cent in the last 175 cases. The mortality for the first 100 cases was 30 per cent; for the fifth 100 cases was 15 per cent; in the last 175 cases it was 9 per cent. The deaths were due chiefly to peritonitis, paralysis of the intestines, degeneration of the heart, embolus and pyelonephritis. It was seldom due to other causes. Weibel emphasizes the fact that there is a rise in mortality which is parallel to an increase in operability, stating that men who operate 80 per cent of their cases may have 20 per cent to 25 per cent mortality. In this connection, we observe that the mortality following radical operation will be much less than that reported in the literature when operations are restricted to early growths and when all others are treated with radium. Wertheim's results for a five-year period of observation are truly remarkable. In all, 863 cases were seen for the series. Of these, 36 refused operation, 447 were inoperable, and 380 were operated by his radical operation. Eight cases died of intercurrent disease and only 1 case escaped observation. There were 160 cases which were free from recurrence at the end of five years' observation. This equals 43 per cent of the cases operated, and 53 per cent of the cases surviving operation. (Weibel insists that one cannot consider cases which die following operation in calculating cure.) In calculating his absolute cures, he considers the series of 863 cases. From these are deducted the 36 that refused operation and 8 that died from intercurrent disease. There remain 819 cases, of which 160 are free from recurrence at the end of a five-year period of observation, thus equaling 19.5 per cent of absolute cures.

There are comparatively few series which are entitled to consideration after the massive statistics of Wertheim. Scheib reviewed the material from the clinics of von Franqué and Kleinhans from 1903 to 1907. He found operative cures for a five-year period in 25 per cent of 149 cases, and absolute cures for a five- to six-year period of 3 per cent to 5 per cent.

Franz and Zinsser, from January, 1904, to January, 1910, had 245 cases of cervical carcinoma; 82 per cent were operable; the primary mortality was 21 per cent. There were 19 cases which survived the five-year period which, therefore, constituted his series for calculation. Only 3 were free from recurrence, a cure of 18.7 per cent. Franz'

report showed that the mortality rises rapidly with an increase in operability. Thus, the mortality was 12.6 per cent in the cases in which the parametrium was not involved, while it was 24.4 per cent in the 82 cases which had infiltrated parametria. The infiltration extended as far as the pelvic wall in 21 cases and in these the mortality was 23 per cent.

Martin obtained an operative cure according to the Waldstein theory, in 19 per cent of 195 cases.

Schottlaender reports von Rosthorn's cases at Gratz, Heidelberg, and Vienna. Only the 85 cases treated at Gratz include cases which have stood for five years. There were 27 cases which had been operated more than five years, in which there was 20 per cent absolute cure. The other cases of the series included 8 cases that were lost during the period of observation, 1 which died of intercurrent disease, 18 which were alive for two and a half years but which had not been followed long enough to be counted as cured, and a 24 per cent operative mortality.

Zweifel's results were recorded by Aulhorn. The operative cures according to Werner's method were 20.46 per cent.

Jacobson, in 1911, made an extensive résumé of the results of operations by American and European surgeons. He collected a total of 2,765 radical abdominal operations. Of these, 2,467 were from European clinics and 298 from American surgeons. He carefully checked the reports and found that all of the operations were radical in the sense that it is used in this article. There were 538 deaths in the series, giving a primary mortality of 19.45 per cent. The Europeans obtained a higher operability and also a higher primary mortality than the Americans, being 65 per cent operability for the Europeans to 35 per cent for the Americans. The mortality was 19.94 per cent for the Europeans and 15.77 per cent for the Americans. The mortality varied considerably among different men. Thus, Doederlein had 30 deaths, or 14.3 per cent in 209 operations; Jacobs had 6 deaths, or 6.4 per cent in 95 cases; Klein had 7 deaths, or 12.8 per cent in 52 operations; Zweifel had 17 deaths, or 10.8 per cent in 192 operations. Occasionally, fairly large series were operated with very little mortality. Doederlein had 2 deaths (5 per cent) for 40 operations; Krönig had 2 deaths (4.2 per cent) in 47 cases; Wertheim had 3 deaths (5.6 per cent) in 53 cases, and Veit had 20 cases without a death.

The percentage of operative cures at the end of the five-year period is given for von Rosthorn as 20 per cent; Veit, 30 per cent; Reinecke, 35 per cent; Wertheim, 58.6 per cent; and Polosson, 60 per cent. The percentage of absolute cures was 2.65 per cent for von Rosthorn; 19.3 per cent for Wertheim; 58.3 per cent for Mackenrodt, five years after operation. In marked contrast to these figures, the Americans obtained

operative cures for the five-year period of only 8.39 per cent, and absolute cures of 1 per cent.

Meyer reviews Doederlein's material from 1902 to 1905. There were 211 cervical carcinomata with an operability of 59.7 per cent. The average primary mortality was 20 per cent, and varied between 36.6 per cent in 1902 to 10.8 per cent in 1905. He gives the results as 29 per cent of operative cures, and 17.1 per cent of absolute cures.

Hofmeier had 393 cases of cervical carcinoma between 1899 and 1910. The operability was 52 per cent. The average mortality was 20 per cent, ranging from 27.6 per cent in the earlier cases to 11.6 at the close of the series; 31.3 per cent survived the operation for five years or more; the absolute cures were 14 per cent. Hofmeier omitted in compilations the cases lost track of and those dead of intercurrent diseases.

From April, 1903, to September, 1904, there were 79 cases of cervical carcinoma at the Jena clinic under Krönig's direction. There were 60 cases operated, or 79 per cent operability, with a primary mortality of 25 per cent. There were living and well 19 cases after a five-year period of observation, giving operative cure of 32 per cent, and absolute cure of 25 per cent. The value of the operation was shown to the author by the fact that 12 of the 19 cases which survived the five-year period had marked infiltration of the parametrium. There were no carcinomatous glands in any of the survivors. Franz succeeded Krönig in Jena and saw 120 cervical cancers between October, 1904, and March, 1907. He was able to operate 87 of these, or 80 per cent operability. The operative mortality was 23 per cent. There survived operation 67 patients, of whom 33 per cent were living and free from recurrence at the end of five years. The operative cure, therefore, was 33 per cent, and the absolute cure 27.5 per cent. Franz believes in high operability and is extremely radical, removing as much parametric tissue as he possibly can. He claims that the wisdom of this procedure is shown by his results since 27.5 per cent absolute cure is greater than Krönig's 25 per cent, or Zweifel's 20.5 per cent, or Wertheim's 18.6 per cent. He refuses to operate only when the cancer has grown through the bladder wall, and considers the parametric infiltration, a solid fixation of the tumor, and extension of the growth to the vagina and rectum do not contra-indicate operation. In this he differs from nearly every other surgeon. When a recurrence takes place, he thinks that it should be removed at the earliest possible moment, and cites the instance of a woman who had five operations for recurrence in the four years after the first vaginal operation in 1905, and yet, at the time of his report, there was no sign of recurrence three years after the last operation.

Pető, in 1913, reports a series of 100 cases operated by Wertheim's method. Sixty-three per cent of his material was operable. The mor-

tality was 14 per cent. Ten cases survived operation for five years and more without recurrence. There were also 31 cases living without recurrence who had not yet stood as cured for five years, although most of these had remained cured between four and five years. Recurrences were noted in 23 cases. There were 13 deaths from intercurrent disease without evidence of recurrence. Twenty cases of the series were lost sight of.

There are comparatively few records of the results of American surgeons. Ries treated, between 1897 and 1910, 32 patients with carcinoma of the cervix. Eleven were not operable. Of the 21 operated, 8 died from the operation. Of the 13 surviving operation, 2 were not operated radically, since the operation could not be completed. Arranging his cases to show the results for five years or more, he found that there were 16 who applied for treatment from thirteen to five years before his report. Of these, he operated 13. One case was counted as lost sight of, although she returned with a recurrence in the external inguinal glands nine years after operation and was operated for a second time and followed for one year. Six died and 6 were alive at the time of his report in 1911, living respectively twelve years, 1 case; eleven years, 1 case; ten years, 1 case; nine years, 2 cases; and seven years, 1 case. In 1912, at a meeting of the American Gynecologic Society, the symposium on uterine cancer brought out fairly representative reports of the results of other operators in America. Cullen, personally, performed 49 Wertheims, with a primary mortality of 11 cases, or 22.4 per cent. There were 26 cases operated for five years or more. Seven of these died from operation, 1 was lost sight of, and 7, or 26.9 per cent were cured for five years. Clark, presenting his figures from the University of Pennsylvania Hospital, reported 36 radical operations with 3 deaths, or 8 per cent. Six cases were lost track of, and 6 survived from four and a half to six years without recurrence. Kelly reports (Neel) 136 cases on which a radical abdominal operation was performed in his clinic with primary mortality of 28 cases, or 20½ per cent. During the five years preceding this report, the percentage of operability was 54 per cent. There were 70 cases in whom five years or more had elapsed since operation. Of these, 9 were lost track of and 61 were traced. One patient died of an intercurrent disease. There were 14 which remained as cured. The percentage of operative cures based upon the number of cases in which the complete operation was done, excluding those lost track of, is 23.3 per cent. Excluding the number of primary deaths (20), 1 case dying from intercurrent disease and the number of cases lost track of (9), there remain 40 cases of which 14 were cured, or 35 per cent.

Sampson reports that 8 of his 25 cases were operated more than five years and thus may be studied. There were 2 primary deaths. Of the 6 surviving operation, 4 are living and well without recurrence for

more than five years. Peterson also reported that 6 of his cases survived operation five years before; of these, 3 are living and well. Tausig collected a number of cases operated by the Wertheim procedure by surgeons of the Mississippi Valley and westward. There were 14 cases which were operated more than five years. There were no primary deaths in the series. Five, or 41.6 per cent, were living and well without recurrence at the end of the five years.

Cobb, in 1915, reports 55 Wertheim radical operations performed at the Massachusetts General Hospital between 1900 and 1914. There were 12 deaths, or 21.8 per cent. Fourteen of the cases were operated more than five years, and of these 7 or 50 per cent, were alive and free from recurrence. Very unfortunately, Cobb presents his results under the general heading of cancer of the uterus, so we cannot say whether the series was comprised entirely of cancer of the cervix or not. He also reports his personal cases during the same period done in the same hospital. There were 31 of these. There were five deaths, or 16.1 per cent. Of the 6 cases which were operated for five years, or more, 5, or 83 per cent, survived the five-year period without recurrence. This splendid series is also not available for critical study because the type of cancer is not stated.

Results of the Radical Vaginal Operation.—Schauta was the chief advocate of this operation. He published, in 1911, the results of his ten years' experience. During this time, 910 cervical carcinomata applied for treatment. Of these, 445 were operated; 44 refused operation; and 421 were inoperable. The primary mortality for the 445 cases was 8.9 per cent. The cases operated during the last three years of the series had only 3.7 per cent mortality. During the first half of the ten-year period, forming his report, 447 cases of cervical carcinoma presented for treatment. Of these, 211 were operated with an operative cure of five years' standing of 39.7 per cent and an absolute cure of 16.6 per cent. Schauta, on the basis of these figures, calls attention to the fact that, while Wertheim's absolute cures are a little less than 2 per cent better than his, this advantage is more than offset by his higher operability (51 per cent in contrast to 48.6 per cent) and his lower operative mortality (8.9 per cent in contrast to Wertheim's 18.6 per cent).

Thorne also records his experience with this operation. During the years 1896 to 1905, 227 cervical cancers presented for treatment. He had an operability of 44.2 per cent, a primary mortality of 5.2 per cent, and an absolute cure of 19.35 per cent.

RESULTS OF LESS EXTENSIVE METHODS

Werder, in 1912, reports his series operated by his cautery method of hysterectomy. As previously stated, the parametria were not removed. Thirty-nine cases were operated more than five years.

Twenty-one of these were vaginal igni-extirpation: 18 were combined vaginal and abdominal operation. Of these, 18, or 46 per cent, survived the five-year period. Five of this group, however, died subsequently—1 after six years from intercurrent disease, and 4 from recurrence. The 4 recurrences are described as follows: 1 after six and a half years from carcinoma of the liver; 1 after six years from involvement of the retroperitoneal glands and spinal cord; 1 after five and a half years from recurrence in the lumbar glands; and 1 after five years, place of recurrence not known. Rearranging his cases up to the time of his report, he found that 13 of the 39 cases ($33\frac{1}{3}$ per cent) were alive and well, 3 having lived eight years or more since the operation; 3, seven years and more; 2, over six years; and 5, over five years. The mortality for this series is not stated. He notes, however, that he had 4 deaths in a series of 78 cases.

Vaginal Hysterectomy.—Von Ott, who is recognized as a very skillful technician, recorded in 1909 his results by the simple vaginal method and contrasted them with the results of the other methods in the following table. It seems worth while in passing to call attention to the fact that the results accredited to Wertheim, Staude, and Schauta are not those of their final compilations, and that few, if any, have equaled von Ott's results with the simple operation.

	Advanced abdominal method (Wertheim)	Advanced vaginal method (Staude)	(Schauta)	Simple vaginal method (von Ott)
Cases operated upon for five years or more.....	116	58	47	191
Deaths following operation.....	27	9	9	4
Mortality.....	23.3%	15.5%	19.1%	2.1%
Cases kept in view for five or more years.....	87	41	34	152
Absolute percentage of cure according to Winter.....	24.7%	23.0%	16.7%	15.5%
Absolute percentage of cure according to Waldstein.....	19.16%	13.5%	15.1%
Frequency of injury to neighboring organs.....	8.9%	11.6%	9.2%	

Treatment of Recurrences Following Operation.—A number of Europeans have advocated the operative treatment of recurrence under certain conditions. Von Rosthorn, in particular, was an advocate of this procedure under favorable conditions. Franz also operates recurrences and cites one case who had had five such operations in the four years following the first one and yet at the time of his report, three years after the last operation, there was no sign of recurrence. E. Zweifel, in 1914, reports 23 cases operated at Jena for recurrences.

There were 31 such operations performed on 20 women, 30 per cent of whom survived without return of the growth for an average of seven and a half years. While there is undoubted justification for such treatment, not only from the results cited above but also from other references in the literature, the treatment is at least debatable. The question, however, is not of paramount importance in this country at the present time, since the majority of cases operated here are really inoperable and the so-called recurrence is but the proliferation of tissue which was not removed at the primary operation. There is a vast difference between removing isolated glands, which subsequently enlarge because of carcinoma, and an attempt made to remove carcinomatous parametria which were left at the first operation.

RADIOTHERAPY

By this term is meant the treatment of disease by X-rays, and by radio-active substances, namely, radium, thorium, and their products. This form of therapy constitutes a most important and interesting addition to the therapeutic armamentarium. Since the discovery of the X-ray in 1895 by Crookes, and subsequently by Roentgen, and the recognition of radio-active substances in 1896 by Henry Becquerel, much investigative work has been done along these lines which has resulted in a radical change in our former conceptions of the properties of matter and energy and the laws of physics and chemistry. Since the isolation of radium by the Curies in 1898, radium and its allied substances have been employed extensively in different fields, and have enjoyed much popularity. The tremendous interest excited by radio-active substances has been reflected in popular literature, and the public has been led to believe that the fight against cancer has been won. In spite of the harm that has resulted from the popular dissemination of such teaching with its false sense of security, it has nevertheless served to stimulate real scientific investigation. This has gradually resulted in an understanding of the action of radium on cells of the human body, and with it has come a better idea concerning the dosage, screening, length of exposure, and the limitations of the treatment. In consequence, the subject is now assuming a definite therapeutic basis.

There are more than thirty elements which are radio-active. These belong chiefly to three groups, namely, uranium, thorium and actinium. Uranium is found in nature as a black oxide, pitch-blende, as uranates in combination with calcium, and in carnotite combined with vanadium. Its radio-activity is due to its association with radium which occurs with it in varied proportions. Radium is more widely disseminated than is generally known; practically all rocks, spring water, and even seawater contain it in infinitesimal amounts.

Radium.—Radium is an element of the strontium barium group. Its properties are quite generally known. It is derived from uranium, and was first isolated commercially from pitch-blende obtained from mines in Austria. At the present time, it is isolated from carnotite, which occurs in considerable amounts in Colorado. It is used as a salt in therapeutics, since the rays which are useful for treatment are derived from disintegration products which are held by the salts.

Thorium.—The almost prohibitive cost of radium has stimulated much popular and scientific interest in thorium, which has been obtained commercially as a byproduct in the manufacture of incandescent gas mantles. It is found as a thorite in North and South Carolina, Brazil, and Ceylon. Its life period is unknown. Occasionally, it is found associated with a relatively high per cent of radium. Employed in therapeutics such as mesothorium, it contains about 25 per cent radium. The activity of mesothorium reaches a maximum in about three years after its manufacture. In twenty years, it has lost half of its activity, and finally its only energy is due to the 25 per cent radium, the latter losing half its power in eighteen hundred years.

Radium Rays and Emanations.—The different types of rays emitted by radio-active substances may be distinguished by observing whether they are deflected in a magnetic field, and by comparing their relative absorption by solids and by gases. It has been proved that there are three different types of rays, which are termed Alpha, Beta and Gamma rays. Radium is constantly giving off rays and a radio-active gas termed emanations. The latter escapes into the air under certain conditions and rapidly disintegrates, passing through a succession of changes known as radium A, B, C₁ and C₂, D, E, and F. Radium A, B, C₁ and C₂, are termed the active deposits of rapid change. Radium D, E, and F are termed the active deposits of slow change. Only the former are of interest from the standpoint of therapeutics. If the radium salt is inclosed in a sealed tube, the disintegration products are practically all retained.

The emanations belong to that class of inert gases which, like nitrogen, do not seem to enter into chemical combination with other elements. They possess the properties of gas, that is, diffusibility, solubility, condensation and liquefaction. They can be transported from point to point by currents of air and can be separated from air or from other gas with which they are mixed by the action of extreme cold. The emanation is radio-active, ionizes air, and discharges electrical bodies, affects photographic plates, and passes through substances opaque for light. Emanation may be compressed into very small glass containers and may be used as a therapeutic agent, since it emits Alpha, Beta and Gamma rays. The Gamma rays are the most valuable ones for therapeutic purposes. They are also derived from radium C₁, and

C₂, and the activity from a therapeutic standpoint is derived from the products of rapid change.

Whereas radium salt loses half its strength in about two thousand years and may be regarded as practically constant for therapeutic purposes, the emanation loses half its strength in 3.8 days, that is, practically one-sixth a day. By appropriate means, radium emanations may be obtained from the radium salt. Treatment by emanation has the great advantage that the size, shape and strength of the applicator may be varied at will. The use of emanation, moreover, avoids chance of losing the expensive element following treatment. Because the emanation is constantly losing its strength, allowance must be made for this fact during the treatment. The radium element, as used therapeutically, is combined as a salt either as chlorid, bromid, or sulphate.

Alpha Rays.—The Alpha ray is a particle of matter or positively charged atom of helium and is discharged at a rate between 1/10 and 1/20 that of the velocity of light. The rays possess but little power of penetration and are arrested by a thin piece of tissue paper or folds of gauze. They produce a marked chemical change, but are not of use practically for treatment except for the most superficial lesions of the skin.

Beta Rays.—The Beta ray is an electron or small particle charged with negative electricity. It is the same as a cathode ray. It moves with the velocity of light, and its mass is equal to about 1/1000th part of a hydrogen atom. These rays are not homogeneous, and for practical purposes are divided into soft, medium, and hard rays, the latter having the greatest power of penetration. They can penetrate nearly 1 centimeter of tissue. The softer rays cannot pass over more than 2 millimeters of lead or 1.2 millimeters of brass, yet the harder rays are of extreme tenacity. It is doubtful whether 1 centimeter of lead will completely arrest them.

Gamma Rays.—Gamma rays are not particles of matter but are vibrations of ether similar to ordinary light. They have an extremely short wave length and a high power of penetration, but are said to be less effective than Alpha or Beta rays in producing chemical changes in the tissues. These rays are not polarized and cannot be deflected from their path. They originate from disturbances of the electric components of atoms and are real electromagnetic waves. As has been already stated, these are the most important rays in radiotherapy.

The Action of Radium.—Wickham can properly be considered the pioneer in the treatment of cancer by radium. He began his work in Paris in 1906, and in 1913 was able to publish the result of the treatment of 1,000 cases of cancer by radium. Dominici, a coworker, developed the principles of filtration. Abbe, in New York, first used radium for the treatment of uterine cancers. The first therapeutic results of radium did not appear to differ from those obtained by a caustic. This

was due to the fact that so little radium was used that there were not enough Gamma rays for therapeutic action, and that the soft rays, which predominate, acted as a caustic. Larger quantities of radioactive substances are used in the modern methods of treatment and are given for a considerable length of time. The older idea that radium was simply an expensive and efficient form of cautery has been disproved as a result of histologic study. There is no doubt that radium has a marked selective action on pathologic tissues, although at the same time it exerts a less marked influence on normal tissue. The Alpha and weak Beta rays produce chemical changes, while the hard Beta and Gamma rays exert selective action upon the tumor or embryonic cells.

The change produced in tissues is due to the activities of the protoplasmic enzymes which are retarded or accelerated, depending on the intensity of radiation. The changes induced in the enzymes are thought to be largely a chemical reaction. Joly attributes the effect on the tissues to the ionizing properties of the rays, a change analogous to the alteration which takes place on exposing a photographic plate. Some believe that the rays act as a stimulus to metabolism, since a small dose accelerates and a strong stimulus retards or prevents all metabolic activity. Others hold that the rays cause a breaking down of tissue with the production of lecithin which is toxic to protoplasm. While we do not know the exact physiologic action on the rays, it is apparent that the alteration produced by them is out of all proportion to the energy liberated. Moreover, a change that has once started may continue for weeks after the primary radiation.

Different types of normal cells vary considerably in their sensitivity to radiation. In order to standardize the amount of tissue alteration, the amount of radiation which will cause an erythema of normal skin is taken as the unit of comparison. It is found that normal tissue, particularly fibrous tissue, is very tolerant. The lymphatic organs are especially sensitive and are easily destroyed, as are the hair follicles, and glands of the skin, and the reproductive glands. The endothelium of the blood vessels may swell up even to occlude the lumen of the smaller vessels. Muscle is more sensitive than is epithelium. Epithelial areas vary in their response to raying, the tongue being more sensitive than the vaginal mucous membrane. Burnam found that the connective tissue of the cervix, bladder, vagina, and even rectum, could bear fairly large doses. He found that the ovaries were injured ten times as easily as normal skin, and that the vaginal wall was four or five times as tolerant as skin. The mucosa of the uterus and the rectum are as tolerant as skin, and the cervix is twenty times more resistant. Young and immature cells, as tumor cells, are much more sensitive than adult, healthy cells, and the sensitivity of tumor cells varies according to their age, development, structure, and situation. Adeno-

carcinoma of the cervix and the body of the uterus is more easily injured than epithelioma. The action of rays on the same type of tumor is not always the same. There will come a period in every growth when the rays will have only a slightly different effect upon the malignant cells than they do upon the surrounding pelvic tissues. It is thought that tumor cells may acquire a certain amount of resistance to radium. It is a clinical fact that many tumors which do not respond to prolonged X-ray treatment will become materially altered and shrunk following exposure to radium. It also is a clinical fact that the most efficacious rays are not those which are the most easily absorbed. The absorption of Gamma rays must be very small, yet they are the most efficient rays for the treatment of tumors.

The chromatin of the cells is most sensitive to the action of radium and soon exhibits conspicuous evidences of degeneration. While there is a marked action upon the protoplasm as well, it is obvious that a cell whose chromatin is either destroyed or injured so seriously that it is incapable of division, is no longer dangerous from the cancer point of view. Tumor cells are either killed or sterilized by the action of proper doses of radium and lose their power of proliferation. Shortly they degenerate, and are replaced by connective tissues, formed for the most part by wandering tissue cells.

Microscopic Appearance of tissues Subjected to Radium.—Microscopic examination of tissues subjected to radium show that the first noticeable change is edema which infiltrates the tissues. The cell shortly increases in size and loses its characteristic form. The nuclei also increase in size with a marked diminution in the distinctness of the nuclear structure. Vacuolization is now noted both in the nucleus and the cell protoplasm, and the tissues are more vascular. Detritus is present, and the cells coalesce into formless masses. The chromatin also gathers into masses which occasionally are so large that they suggest artifacts. Surrounding the degenerated area is a zone of active leukocytosis. The carcinomatous detritus is finally carried away by phagocytes, and the empty spaces are filled in by fibrous tissue. On the periphery of the treated zone, the destruction of cells is not usually complete. There may be found isolated or grouped cancer cells. The subsequent growth of the fibrous tissue becomes an important factor in the reparative changes. If the radiation has consisted too largely of Beta rays, the normal tissues may be broken down, and the reparative changes either postponed or entirely prevented. This frequently leads to fistula formation. Some histologic types of cervical carcinoma are more susceptible to radiation than are others. For example, the basal cell type of epithelioma is very susceptible to radio-activity. The papillary type of epithelial tumor which is everted in form and in which glandular metastases are relatively late is also specially susceptible to radium.

Technic.—Dosage is expressed in terms of the products of milligrams of radium or millicuries of emanations and the number of hours it is applied. The product is the so-called milligram or millicurie hours. Thus, 200 milligrams or millicuries applied for fifteen hours gives a dosage of 3,000 milligram or millicurie hours. Also, 50 milligrams for thirty hours, repeated in a few days, would give the same total of milligram hours. Yet the physiologic action will not necessarily be the same. A gram of radium and a curie of radium emanation has the same Gamma ray activity. Corresponding to the multiples of the gram and the curie, are the milligrams and millicuries which are used for measuring the activity of the salts and emanations respectively. In order that records may permit of comparison, it is necessary to state: (1) the amount of radium element or emanation used; (2) the exact method of screening; (3) the distance between the container and the tumor; (4) the hours of each treatment; (5) the intervals between treatments; and (6) the total number of hours in each series.

In order to obtain the proper therapeutic effect from radium, the pathologic tissues must be radiated with a dose sufficient to kill them but not sufficient to destroy the normal adjacent tissues. The various rays are absorbed by the tissues in a constant, uniform manner, even if the hard Beta and the Gamma rays differ in their power of penetration. That is to say, in a given thickness of tissues, there is a uniform percentage of absorption of the rays which have passed through. It is generally stated that 8 per cent of the Beta rays are absorbed by each tenth of 1 millimeter thickness of tissue, and 5 per cent of the Gamma rays by each centimeter of tissue. It is also important to know the intensity of radiation on any surface, since intensity of radiation as in all spherical dispersion, varies inversely as the square of the distance from the source. For example, the intensity of radiation from radium 1 millimeter distant from a 1 millimeter square surface is 625 times that from the same radium upon the same tissue moved 25 millimeters away. It is obvious from this why the physiological effect of the Gamma ray is limited to distances of 2 to 3 centimeters. While some Gamma rays act at greater distance, they are too few to cause evident results. Some, however, claim that Gamma rays are effectual at greater limits, and Bumm believes that they may be efficient as far as 4 centimeters.

In gynecology, the radium is generally used in tubes, either as a salt, or the emanation. It is inclosed in a glass capsule, hermetically sealed, which cuts off the Alpha rays. This, in turn, is covered by a similar container of silver or platinum. Other filters are necessary in order to cut off all the Beta rays. The following screens are supposed to suffice and to be more or less equal to each other: silver, 1 millimeter; brass, 1.3 millimeters; steel, 1.4 millimeters; lead, 1.5 to 2 millimeters; gold, .6 millimeter; and platinum, .5 millimeter. It is probable that Beta

rays, when passing through lead filters, break up, at least in part, and give rise to more secondary rays than are noted with other screens. This is very likely to cauterize the surrounding tissues. These secondary rays, or *rayons de Sagnac*, may be cut off by inclosing the radium containers and their screens in a black rubber tubing or hard rubber capsule whose walls are 2 to 3 millimeters thick. The physiologic effect from the rays of the radio-active substance is due to the photo-electron action, that is, the liberation of negative electrons in the tissue. Gamma rays produce at least part of their effect by the action of secondary Beta rays which result when the Gamma rays pass through cellular tissue. Since the primary Beta rays are readily absorbed, they are useful only in the treatment of superficial growths at a very few millimeters thickness. Since the Gamma rays have greater penetrating power, they produce secondary Beta rays throughout a considerable depth of tissue; consequently they are useful in the treatment of deep lesions. When employing the primary Beta ray, the Gamma ray is negligible, since the latter are comparatively few. The relative proportion of Beta and Gamma rays is as 95 is to 5. When we desire to use chiefly the Gamma ray, the Beta ray should be screened off by metal filters.

Theoretically, cancer of the uterine cervix offers a splendid opportunity for treatment by radiation, since the radium capsule can be inserted in the cervix in the very center of the carcinomatous area when it will radiate through the center of the pelvis. The pelvic axis is approximately 12 centimeters in its diameter, so rays 6 centimeters in length would completely radiate the entire pelvic cavity. Unfortunately, radium in ordinary dosage has power probably to kill only the cancer cells which lie 2 or 3 centimeters away. Beyond this, there is always the chance that cancer cells may be stimulated to activity by rays that are too weak or too few to kill. The bladder and rectum may be injured by treatment, since they are less than 2 centimeters distant from the cervical canal if the organs are empty. Should they be filled, they are much closer to the cervix. In order to avoid injury, they should be empty and held as far away from the cervix as is possible. The ureter is also close enough to sustain injury.

Unfortunately, there is no agreement as to technic or dosage in the radium treatment of cervical cancers, save that nearly all agree that good results may not be obtained with less than 50 milligrams or millicuries of radium. There are two schools, one believing in a minimal dosage, repeated to get accumulative effects upon the cancer cell but subliminal as far as the normal tissues; the other argues that the best chance of attacking the cancer is by massive doses at the first treatment, although few longer advise the use of as much as a gram even for a short time except rarely for cross-fire. Both schools agree that the cervix should be gently dilated or burned open sufficiently to admit

the radium capsule. Nearly all have abandoned preliminary cauterization or curetting.

Schmitz is the advocate of the small doses given by the fractional method. In order to prevent fistula formation which is almost certain to result in case the bladder and rectum are burned to a serious degree, he gives doses which he believes will kill the cancer cell but not cause serious injury to the bladder or rectal walls. He calculates that 600 milligram element hours obtained by 50 milligrams of radium element maintained in position for twelve hours, will cause a second degree burn of these organs but that a ten-hour application of 50 milligrams of the radium element or 500 milligram element hours will kill the cancer cells but not injure the bladder or rectum. He believes that the normal cells of these organs which have not been burned to the second degree recover so rapidly that they will withstand another similar treatment after an interval of twenty-four hours. He gives, therefore, a treatment of 500 milligram element hours daily for seven successive days, making a total dosage of 3,500 milligram element hours which he claims will cause a degeneration of all carcinoma cells as far out as the bony pelvic wall. To the latter view, we cannot subscribe, since there is no evidence to cause us to believe that Gamma rays from 50 milligrams of radium are effective at more than 3 or 4 centimeters. Schmitz states that the bladder is not injured by his method, as may be proved by cystoscopic examinations made at ten-day intervals during the period the radium is causing changes, that is, six weeks. He uses two tubes of 25 milligrams of the radium element in the form of the insoluble sulphate, each of which is packed in a cylinder of glass of an outer diameter of 2 millimeters and a length of 6 millimeters. These cylinders are, in turn, inserted in silver capsules 1.75 centimeters long with a wall 0.5 millimeter thick. These two capsules are placed tandem in a brass tube with a wall 0.7 millimeter in thickness. The total metal screen 1.2 millimeters thick effectually absorbs Beta radiation. The Sagnac rays arising in the metal filter are absorbed by a pure black rubber tubing 3 millimeters thick in which the radium carriers are contained when they are placed in the cervix. The vagina should be packed with gauze. Schmitz reports his results in 1920, but since none of his cases have stood for five years, they cannot be considered at this time. Preliminary to the treatment a self-retaining catheter is placed in the bladder and the bowels are emptied by enema.

The other view is represented by the various workers in the Memorial Institute in the city of New York. They advise that 3 tubes of 50 milligrams emanation properly screened in a manner similar to the above and arranged end to end, be placed in the uterocervical canal for twenty hours. This gives a cross-fire on the upper and lower margins of the growth as well as direct radiations to its center. Added cross-fire is obtained by placing three tubes containing the same

amount of emanations against the cervical ulcer. They are held in position by a mold of dental modeling compound. This also holds the bladder and rectum back in place. The treatment is given for 20 hours, or a total of 6,000 millicurie hours, which is obtained by 3,000 millicurie hours from the tubes within the uterus and 3,000 millicurie hours placed against the cervix.

The majority of workers believe that there is no advantage in using primary Beta rays and advise a screen sufficiently heavy to eliminate all but a pure Gamma radiation. Others, however, feel that the hard Beta rays are also useful. Local treatment, especially for small cancerous nodules in the vagina, may be obtained from a number of bare tubes containing 2 to 5 millicuries emanations placed about 1 centimeter apart directly in the growth. The rectum should be screened by packing the vagina with gauze to prevent the reaction which otherwise would occur.

Some, as Turner, have advocated large doses even to 10,000 to 15,000 millicurie hours for a primary treatment. Turner claims (1920) that he has never seen bad results following this dosage. The treatment, however, is much more severe than that given by the American gynecologists who have much radium at their disposal.

Personally, we have used both the fractional and the single large-dose methods. For two years, we used from 50 to 90 milligrams of the radium element placed in the crater and maintained in position long enough to give a primary dose of 1,200 to 1,500 milligram hours. The treatment was repeated weekly for four or five times. The results were quite as satisfactory as those yet obtained by our present plan of treating with 150 to 200 millicuries applied in several tubes placed in the cervix, a method which we have used for three years. We have rejected as useless augmenting this treatment with bare needles of 2 to 5 millicurie strength in the margin of the ulcers. We apply the tubes while the patient is anesthetized. In addition to the glass capsule, there is a screen of 0.5 millimeter silver and 1.2 millimeters of brass and a hard rubber container 3 millimeters thick. The bladder and rectum, which have been emptied before the treatment, are held apart by the dental modeling compound which fills the upper part of the vagina. Rubber dam and gauze are also used occasionally as accessory filters. *Personally, we feel that it is often dangerous to dilate the cervix for the introduction of the radium.* We feel that it is often responsible for metastases and the spread of the growth. Occasionally a cavity may be made with a cautery, otherwise the radium should be placed in the crater unless the cervix is open and may be dilated without trauma.

Cross-fire.—Since the rays from moderate doses of radium applied directly at one point in the cervix produce satisfactory results through only 2 or 3 centimeters of tissue, it follows that supplementary treat-

ment is necessary to kill the cancerous cells that lie farther out in the pelvis. Some sought to obtain a cross-fire by placing radium in the rectum, and by radiating the parametria with rays filtered through heavy gold screens made from a twenty-dollar piece. This method has been abandoned. Cross-fire may be obtained with very heavy doses (a gram or more) of emanations, by radiating over a large number of different areas on the abdomen and pelvic wall to the parametric wings and the glandular areas. This method has its basis in the fact that all Gamma rays are not of equal length. The longer rays may be utilized, if the radium is applied at some distance from the skin, and the weaker and shorter rays are cut off by heavy screens. It is believed that when radium is applied 12 centimeters from the skin surface that 80 per cent of the Gamma rays will reach 1 centimeter below the surface; 38.5 per cent will reach 5 centimeters below; and approximately 20 per cent will reach 9 centimeters below. Therefore, by radiating through five portals of entry, we should produce at the depth of 9 centimeters the same intensity of dosage obtained in the tissues under one of the five points of application. The practical difficulty is occasioned by the fact that large amounts of radium are necessary to accomplish the results, since only 5 per cent of the heavy rays are Gamma rays, and, of these, only a few are sufficiently strong to cause proper reaction 9 centimeters down in the pelvis.

Amreich, in 1921, called attention to the fact that the uterus and broad ligament parametric structures lie like a butterfly within the pelvis. Seeking to reach the farthest tip of parametric wings, he introduces radium tubes through a tunnel in the obturator foramen on both sides. This technic has also been used by Nordentoft, in 1921, for which he claims many advantages, since the parametria and sacro-uterine ligaments are reached from the side. On paper, it seems like risky treatment.

Others are turning their attention to the *X-ray as a means of cross-fire* in the parametrium. Since the introduction of the Coolidge tube, the X-ray has been used again for the treatment of cancer, although only supplementary to radium or to operation. Few believe that the X-ray is a rational procedure as a primary measure. Moreover, unless the treatment is systematically and judiciously used, it is likely to be not only a waste of time, but possibly harmful as well, since it may stimulate cell proliferation, as do minimal doses of radium. Large doses may, of course, cause serious burns. In an individual of ordinary build, a maximum dose of deeply penetrating and carefully filtered rays must be introduced through seven to ten ports of entry at the skin surface in order to be at all destructive to cancer cells in the pelvis. In the event of metastases, there should be thirty to fifty such treatments made from every possible direction into the pelvis (Pancoast). Such extensive and intensive treatment is bound to exert some effect upon the

intestinal tract and may even do some harm occasionally, although this is not to be considered in comparison with the harm which results from the growth. The patient should be fully acquainted with the situation, however, since suits arising from X-ray burns are unfortunately common. Personally, we have not seen good results following cross-fire with X-ray, even where it had been directly applied through the vagina. Skinner, in 1920, claims that cases which early exhibit a tanning of the skin as the result of the X-ray treatment seem to offer the best prognosis. He states that even variations in technic did not produce tanning in the cases that were losing ground.

Complications.—Patients occasionally present some fever and have nausea and vomiting shortly following radium treatment. In our experience, this has been a very rare event. More serious is the pain which occasionally follows treatment in spite of every precaution. We have noted this, resulting for the most part, from burns of the rectum. In a small per cent of cases, notwithstanding every possible care in protecting the rectum, a very acute proctitis follows. Mucus and blood may be discharged, and the pain may be so severe as to require hypnotics. It may result even though the radium is completely inclosed within the cervical canal. In a majority of cases, a mucilaginous suspension of bismuth subnitrate by rectal injection may be quite sufficient to soothe the pain. It may, however, be so severe as to require opium. We are particularly impressed with the fact that burns either of the rectum or the fibrosis resulting after massive treatment of the uterosacral ligaments may, in the process of contraction, be sufficient even to cause intestinal obstruction. The majority of men agree that large initial doses of radium are likely to cause pain from compression of the nerves by the resulting cicatrix. Others state that particularly heavy screening sufficient to exclude all the Beta rays will do much to avoid pain. However, in a series of 58 inoperable cervical cancers treated by us with divided doses, each of 1,200 to 1,500 milligram hours, pain was conspicuous by its absence, except in the few cases in which fistulae developed.

Fistulae form a very distressing complication. Many, but by no means all, may be charged to the radium, since they may well result from the breaking down of cancerous strands which have invaded the bladder or rectal walls. While it is perfectly certain that this terminal event will occur in a large number of cancer patients which are not treated with radium, we believe at the same time that a man beginning radium work will see more fistulae early in the series than he will later. Pyometra is a common sequence and may best be treated by sounding the uterus occasionally with rubber or metal sounds.

Results of Radium Treatment.—The exact value of radium in the treatment of uterine cancers has not yet been definitely ascertained. Nearly all agree, however, that it is not best adapted for the treatment

of cancers of the uterine body and fundus, since these cases do better with operation. It is difficult to clearly define the position of radium as a therapeutic measure in cancers of the uterine cervix because of the variations in the type of tumor, the amount of involvement, the variations in dosage, the duration of the application, the technic and other variables which cannot yet be accurately controlled. All agree that soft, medullary growths are more easily influenced than harder growths and adenocarcinomata. There is no doubt, however, that radium has a palliative action in the treatment of inoperable tumors which is not equaled by any other type of treatment at the present time. It may also be better than surgery for border-line cases. Some have become most enthusiastic about its possibilities and would extend its use to operable cervical growths, and thus supplant surgery. Yet the careful student will remember that the status of surgery in cervical cancer is only now being clearly defined after the observation of many thousands of cases which were treated by truly radical operations during the past twenty years. Before the results of radium can be compared with those of surgery, it is necessary that all cases treated by radium should be followed in proper classifications for the five-year period just as has been done in surgery. At the present time, there are few statistics which have met this requirement. The present literature fairly teems with the reports of immediate results of radium treatment. Nearly every radium institute in the country is sending forth papers recording cases which have been clinically cured for periods of three months, six months, a year, or a year and a half. This, of course, may mean nothing save that the ulcer has temporarily disappeared. The sane man will postpone his judgment until sufficient data has accumulated upon which we may form an opinion based on facts, and not on hope. The majority of men writing from the standpoint of radium urge that this treatment is practically without mortality as if this were the most important consideration. While no surgeon is especially desirous of doing operations which are attended with 10 per cent to 30 per cent mortality, he is at least interested in the permanent cure. The majority of writers lose sight of the fact that cervical cancers invariably kill unless the growth is completely eradicated. Surgical literature clearly indicates that only early growths permit of cure save in very exceptional instances, since the final results of extensive operations on border-line cases as a class are not good. Consequently there is a broad field for radium in the class of cases where surgery fails, without extending it to other than the operable cases, which by reason of systemic disease cannot undergo operation. Few thinking individuals afflicted with cancer would deliberately choose to prolong their lives for a very few years, if there was every certainty that they would finally succumb to cancer, provided they had a reasonable chance of permanent cure by operation without dis-

tressing sequelae. The clear fact that stands out in the literature of cancer of the cervix is that approximately 50 per cent of operable growths may be permanently cured by surgical measures. The facts are not yet known concerning radium.

Properly speaking, we should consider the results of the radium treatment of cervical carcinoma in the four stages, that is, the operable, border-line, inoperable, and recurrent cases.

Treatment of Operable Cervical Carcinoma by Radium.—The Germans have long been enthusiastic on the value of radiotherapy, but there have been no available statistics until the last year. In 1919, Bumm presented his results between the years 1913 and 1915 summarized as follows: during the year 1913, he had 14 operable cervical carcinomata which he radiated (radium or mesothorium) and did not operate. Of these, 28.5 per cent have remained cured for fully five years. In 1914, there were 20 operable cases which were radiated and not operated. Of these, 20 per cent remained cured between four and five years. In 1915, out of 40 operable cervical carcinoma, 55 per cent remained cured for a period between three and four years. The operative mortality for cancer of the cervix treated by radical operation was 13.8 per cent for 203 cases treated between 1911 and 1915. Of 157 cases operated between 1911 and 1913 in his clinic, 77 were well, after periods from six to eight years or a cure of 49 per cent. Bumm emphasized the fact that the percentage of cures after radium in operable and border-line cases of carcinoma of the cervix was one-third less than that obtained by operation at the end of six years. When the cases are only observed for a period of three years (1915 series), the results of radiation surpass those of operation in cervical cancer, since 55 per cent of the operable cases treated by radium remained well. It has been stated that if there are recurrences following radium they will occur within the first year, if they are going to recur at all. Bumm, however, has had many instances of recurrence in the second and third years after radium. As a result of his investigation, he believes that operation will give better results than radium, when the cases are early and the patient is in reasonably good physical condition. Bailey and Quimby, in 1922, report one operable case (a very early growth) which was indicated and not operated and which remained cured for five years.

Treatment of Border-line Carcinoma by Radium.—There is nearly universal agreement that this type of case can be better treated with radium than by surgery, since the latter rarely cures more than 10 per cent to 15 per cent of the cases in which it is attempted. While some, as Bumm, have obtained distinctly favorable results with surgery, the majority have not done so. There is extensive involvement of the cervix in these cases and the growth has usually extended to the vagina and parametrium so that the uterus is fixed, at least on one

side. With a properly adjusted and properly screened dosage, radium does far more than may be accomplished by surgery and without appreciable mortality. On the contrary, the mortality following operation is considerable in this group of cases. Not every border-line case, however, reacts favorably to radium. Occasionally, we have seen cases which formerly we would have operated show no response whatever to radiation. Since the ulcer alone presented, the original type of the growth could not be determined.

Bumm, during the years 1913, 1914, and 1915, respectively, treated 22, 21, and 38 cases of border-line cervical carcinoma with radium only, obtaining the following percentage of cures at the time of his report printed in 1919, but prepared in 1918: 23 per cent for five years; 19 per cent between four and five years; and 39 per cent between three and four years.

Treatment of Inoperable Carcinoma.—In inoperable cases, excellent palliative results have been obtained by radium, with the control of hemorrhage, discharge and the retrogression of the growth. Occasionally, however, particularly in the advanced cases in which death is a matter of a few months, the treatment seems to aggravate the condition and bring on the end sooner. There are numerous instances of necrotic cauliflower cervical cancers which project into the vaginal canal, which have produced a severe anemia, toxemia, and even cachexia because of hemorrhage and infection. In many cases, radiation of these growths has promptly stopped the bleeding and restored the patient to a normal condition for a considerable period of time. We have seen a number of this type who remained well for two or more years before they succumbed to the disease. Some cases with soft, medullary growths even appear as if they might remain cured. The difficulty in the treatment of these cases is that the growth has approached closely the rectum or bladder. Radium, therefore, is very likely to produce a fistula in event of massive doses. If minimal doses are given, it seems reasonable to believe that the ulcer will be cleaned up, but that the tumor will proceed to grow along its advancing edges on the intra-abdominal side. The most that can be expected in the inoperable growths is that radium will produce a local cure, that is, a cure of the ulcer, and arrest of the hemorrhage and infection. We often overlook the fact that the symptoms of cancer, before the advent of pain and cachexia, are due to the infected ulcer. Curing the ulcer, therefore, produces remarkable results in the general well-being of the patient. Unfortunately, it does not follow that the disease is arrested when the ulcer has been cured.

Bumm treated 42 cases of inoperable carcinoma by radium in 1913. In 1919, 2 were still living, or 4.7 per cent of cure. During 1914, he had 36 inoperable cases with 2 four- to five-year cures, or 5.5 per cent.

In 1915, there were 49 cases. At the time of his report, in 1919, there were 5, or 5 per cent, still classed as cured for three to four years.

There is as yet no other well-controlled series which may be compared with Bumm's reports in which the cases are grouped so that they may permit of comparison with others, with the exception of Bailey's smaller series which appeared in 1922. Within the last year, however, there have been a number of reports of small series of cases which have remained cured for five years. Heyman reports, in 1920, 26 cases from Scandinavia that were treated with radium in 1914. Of these, 7 remained cured in 1919. Unfortunately, he did not state the type of cancers nor give other data save that 85 per cent of this series together with 40 cases which were observed in 1915 and had not yet stood for five years, were inoperable. Hansen, in Copenhagen, in 1920, reports 27.3 per cent of cure for a five-year period in 66 cases, most of which were inoperable. Recasens, in Madrid, in 1919, claims several cases, which were supposed to have been inoperable, remained free from recurrence for five years. There are no reports of five-year cures in America, save for the few cases noted by Ransohoff and Clark. Ransohoff, in 1920, reports 1 operable case which remained free from recurrence after radiation for five years and 1 operable and 1 inoperable case which were also without recurrence at the end of four and a half years, although the last case presented a rectovaginal fistula. Clark, in 1920, reports 1 of 9 inoperable cervical carcinomata which remained free from recurrence, after radiation, for five years. Bailey reports (1922) that none of his 15 cases of advanced cervical cancer, treated in 1915, survived five years. Two of the 15 cases which were treated by the Percy heat method, and then radiated, survived five years. Several cases, however, had a slough of the pelvic tissues in consequence of the ligation of the uterine vessels.

There are numerous observers who report cases cured for four years, yet these cannot be considered at the present time, since they have not yet stood for the five-year period. We have quoted Bumm's four-year cases merely, since they admit of comparison with his five-year series.

Treatment of Recurrences Following Operation.—The treatment of growths which have recurred after operation is nearly uniformly unsatisfactory. In addition to the fact that cures are most unlikely, there is a real danger of injuring the bladder and rectum by radiation, since these structures have been brought close together after the uterus has been removed. When cancer cells are left in the vaginal wall, they may be killed with radium, yet if there are cancer masses in the parametrium, there is less chance of their control. None of the 26 cases treated by us survived two years after the advent of recurrence. The majority of this group were operated by others, chiefly by incomplete vaginal hysterectomies. Some, however, followed Wertheim

operations which we ourselves performed and which we felt were truly radical at the time of operation. Nearly all presented large recurrences in the pelvis. Schmitz, however, has 1 case in his series of 50 such cases that is still living three years and nine months; also 2 cases that lived for more than two years after the beginning of treatment. Bumm, in 1913, treated 25 recurrences after operation. None were living in 1918. He had 37 cases in 1914, of which 5, or 13.5 per cent, were living between four and five years at the time of his report. There were 12 cases in his series in 1915, of whom none remained alive at the end of three years.

The Question of Operating Cases which Appear to Have Been Made Operable by Radium Treatment.—There is as yet no unanimity of opinion concerning the value of operating this type of case. The majority believe that it should not be done because of the chance that carcinoma cells which have been encompassed by scar tissue may escape during the operation and resume their growth. Clark, especially, urges that patients which appear to have been cured by radium should be let alone. Schmitz, and others, agree with him. Some state to the contrary that if the cells which remain alive in the midst of connective tissues are not removed, they will begin to grow again, and finally break through their fibrous capsule and subsequently kill. In this connection, we should recall the experience of Bumm, and others, which shows that, even though the cancer cells in the uterus have been killed by radiation, the lymphatic glands may contain cancer cells which are alive, and which can be removed only by surgical procedure. Practically, however, operation is extremely difficult and it may be well-nigh impossible to liberate the ureters from the dense mass of fibrous tissue which has resulted from the radiation. The glands, moreover, may be so firmly attached to the vessel wall that an attempt to remove them will be followed by serious consequences. Personally, we have operated 6 cases in which inoperable growths were apparently made operable by radiation. As a result of this experience, we believe in the policy of noninterference. One case, especially, was extremely interesting. The patient had a large mass which nearly filled the pelvis at the time of the first treatment. Within three months, it had disappeared almost completely following five weekly treatments, each of 1,200 milligram hours. We then attempted a removal. The parametria were dense and brawny. Both ureters had been converted into hydro-ureters. The first freed without difficulty. In attempting to free the second hydro-ureter, the uterus was torn across the stump of the cervix. One hundred milligrams of radium was placed in the cavity, and the peritoneal cover was completed. The radium was left in place for twelve hours. In spite of this astonishing accident, the patient is living three and a half years after. Degenerated cancer cells

were found in veins in the margins of the cervix. The rest of the tissue was fibrosed.

Radium Treatment Preliminary to Operation.—The impression is constantly growing that radium may be safely used as a preliminary measure before the operation of early cases. Since dense adhesions result four or five weeks after radiation, the majority of men operate ten days after radium at a time when the carcinoma cells are breaking down and there is penetration by the lymphocytes. Edema is still present. Theoretically, this should reduce the chances that carcinoma cells may be detached from their implantation and escape into the lymphatics during the operative removal.

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CHAPTER X

CARCINOMA AND SARCOMA OF THE UTERINE BODY

Carcinoma — Classification — Frequency—Etiology—Age—Appearance and form—Microscopic appearance — Method of growth — Metastasis — Complications — Symptoms — Diagnosis—Treatment—Comparison of types of operation—Radium. Sarcoma of the Uterus — Frequency—Etiology—Age—Location of tumor — Classification — Types — Histology—Sarcoma of the cervix—Types—Mixed forms—Method of extension—Complications—Symptoms—Hemorrhage—Pain—Leukorrhea—Sarcoma of the uterine wall—Sarcoma of endometrium—Sarcoma of cervix—Diagnosis—Prognosis—Treatment.

CARCINOMA OF THE UTERINE BODY

Carcinomata of the uterine body are practically without exception adenocarcinomata. They are nearly all primary. In marked contrast to carcinoma of the cervix, carcinoma of the body of the uterus gives symptoms early, does not tend to invade the underlying structures until the symptoms are well established, and does not give rise to metastases, as a rule, until late in its course. For these reasons, the disease may be cured by hysterectomy in the very great majority of cases.

Classification.—The adenocarcinoma may arise from the surface epithelium of the endometrium, or from the glands, or may develop in the same tissues on uterine polyps. Just as in carcinoma of the cervix, there may be everting or inverting types. A few cases of squamous cell carcinoma of the body of the uterus have been reported as primary growths. This condition is at least extremely rare and there is considerable controversy in regard to it. This phase of the question has been discussed on page 187. Some authors have divided carcinoma of the endometrium into the headings, columnar carcinoma, adenocarcinoma, and malignant adenoma. This classification will not be followed. The tumors are usually primary, although they may develop from metastases from growths primary in other parts of the uterus or from contiguous organs.

Frequency.—With more exact methods of observation, the disease has been found more frequently than was first indicated by the literature, although it varies considerably in different localities. In America, Cullen found that 25 per cent of 176 cancers of the uterus were cancers of the uterine body. Peterson found 16 per cent in 107 cases. Baldy

saw only 24 cancers of the uterine body in sixteen years in Philadelphia. In a series of 98 uterine cancers, we found 8 that were cancers of the uterine body. Roger Williams, in Great Britain, found only 2 cases in 100 cancers of the uterus; Wilson, 5.6 per cent of his series in Birmingham. In Germany, Scheib in 1909 found 27 cancers of the uterine body in 531 cancers of the uterus (5 per cent); Aulhorn, in 1910, reported 5 per cent in a series of 641 cancers of the uterus; Knauer found 2 per cent in 1,374 uterine cancers; Krukenberg, 6.7 per cent in 848 cases; Freund, Sr., 7.9 per cent in 227 cases; Kuestner, 9.4 per cent in 234 cases; Offergeld, 5 per cent of uterine cancers; Hofmeier, 3.4 per cent of 812 cancers; Winter, 12 per cent in 210 cancers. Of the uterine cancers which have been removed by operation, Rouffart found that 10 per cent were cancers of the uterine body; Reipen, 7 per cent; Blau, 12 per cent; Waldstein, 16 per cent; Meyer, 17 per cent. Wertheim saw only 70 cases as opposed to more than 1,500 cancers of the cervix (4.5 per cent). Sixty-seven of these were operated while only 714 of cancers of the cervix were operated. The relative frequency of uterine cancers which were operated in Wertheim's clinic was 9.5 cancers of the uterine body to 100 cancers of the cervix.

Etiology.—The etiology is not known. The various theories which have been advanced for cancer in general have been advocated for uterine cancer. These are reviewed on page 177. The predisposing causes are not identical with those of cervical carcinoma. Thus, pregnancy does not seem to be a predisposing factor in cancer of the uterine body, although there is no doubt that it is such in cancer of the cervix. Cancer of the uterine body often occurs in nulliparous women. Gusserow emphasized this in his early reports. Weibel found that one-fourth of Wertheim's cases had never been pregnant and that 20 per cent had been pregnant but once. Wilson states that there was an average of two and a half pregnancies to each of his 56 cases, which was far less than that found in his series of cancer of the cervix. In about one-third of his cases, the last pregnancy had been twenty or more years before the development of symptoms; the interval was between forty and fifty years in several cases. The frequent association of adenocarcinoma of the body of the uterus with fibroids has been emphasized, and it is possible that the changes in the endometrium induced by fibroids may occasionally be responsible for the malignant condition.

Age.—Carcinoma of the body of the uterus usually occurs after the menopause. Roger Williams, analyzing 500 cases, found more cases between fifty and sixty years than in any other decade. Wilson, in tabulating his 56 cases, found that the youngest was forty-seven years and the oldest seventy-six, while 49 cases occurred between forty-five and sixty-five. While the disease may occur in women who are comparatively young, it does not do so as frequently as cancer of

the cervix. Wertheim's youngest case was thirty-two years. He had only one other under forty. Yet Reipen reported one of twenty years, and Engelhorn one of twenty-two years.

Appearance and Form.—Adenocarcinoma may commence at any point within the uterine cavity. It rarely begins at any one definite point, and even the very earliest stages usually show a rather widespread development of the disease. On sectioning the uterus, the well-advanced growth presents a soft, fairly homogeneous whitish-yellow mass which stands out in sharp contrast to the surrounding muscle. Necrotic areas are not uncommon. On closer inspection, at the edges of the growth the mass will be found to consist of delicate, fingerlike processes which give it a somewhat shaggy appearance. The older polypoid processes may appear as a branched or treelike growth consisting of several main stems and numerous offshoots, and with delicate, fingerlike processes as terminal branches. The tumor is confined almost invariably to the body of the uterus, and rarely extends into the cervix.

Carcinoma which develops from the surface epithelium presents, at first, little mounds of cells developing on the surface. They are composed of two or three, or even more, layers of epithelial cells which, apart from occasional swelling of their nuclei, show nothing abnormal. They are devoid of a supporting stroma. Presently, the little outgrowths become longer and the stroma develops from the underlying tissue, carrying with it loops of blood vessels. The stroma varies considerably, being scanty in some cases and extremely well-developed in others. The epithelial cells are usually much enlarged and irregular. The nuclei are large, irregular, and stained deeply. Occasionally, the epithelium covering the fingerlike processes proliferates and forms glandlike structures. The shape of the polypoid processes varies considerably; sometimes they have crenated margins and are covered by many layers of epithelial cells of fairly uniform size; occasionally they are finely branched and the terminal offshoots consist entirely of epithelial threads; often the margins of the papillae are crenated, showing depressions or bays along their edges. Polymorphic leukocytes are usually found in the subadjacent tissues.

This type of growth was classed by Gebhard and Winter as the evertting form.

Growths which develop in the glands of the endometrium present a similar picture in their earliest phases. The masses are composed of cells, five or six layers deep, which presently assume an atypical glandular appearance. The cells may vary greatly in size, although usually they are much enlarged. Their nuclei are also vesicular and stain rather faintly. Other types of cells may be seen. Occasionally there are parallel rows of gland epithelium, the cells of which are small, their nuclei large and stain intensely, resembling cells seen in chorio-

epithelioma. The gland epithelium sometimes fills the entire cavity and assumes an appearance strongly suggesting the cells of the squamous carcinoma. Mitotic figures and the tendency to invade is seen in each type of carcinoma of the uterine body. Vacuolization and leukocytic infiltration are present in nearly all well-developed cases.

Either of the two types of growth may occur in the carcinoma which develops in uterine polyps of the body of the uterus.

Method of Growth.—The tumor early develops in the plane of least resistance and may not invade deeply the underlying tissues until it has been well developed locally. Early growths may appear to be limited to the superficial portions of the endometrium, yet cancerous areas can be demonstrated usually in the depths. A few tumors have been reported which were so definitely circumscribed that they appeared to have been cured by curetting. Just as in cervical cancer, the division of everting and inverting types is possible only in the early stages. There is usually some infiltration of the underlying tissues by the cancer cells. Yet the tumor extends slowly into the muscular coat, usually in an irregular fashion, and does not reach the peritoneal covering until late in the disease and only after the entire uterine cavity has been replaced by cancerous tissue. It is thought that this slow invasion is due to the atrophy of the uterine wall and the impairment of its lymphatic drainage in consequence of the menopause. Yet metastases may occur through the lymph streams and later through the blood vessels, although they develop much more slowly than in cancers of the cervix. Cancers of the fundus proper drain through the lymphatics of the upper broad ligament and involve both the inguinal and the pelvic glands. Weibel, in 1913, presented the results of the study as to the method of metastases for cancer of the corpus in Wertheim's clinic. He does not share the general opinion that the lymph glands are seldom involved in carcinoma of the body of the uterus. Carcinomatous glands were found 5 times in 31 laparotomies (16 per cent). Since no particular attempt was made to find involved glands in some of the earlier cases, it does not seem improbable that these figures are lower than the actual fact. It is of interest that the inguinal glands were only involved in 2 cases, probably because of the small size of the lymphatics running along the round ligaments in this series of cases. He found that the iliac and lumbar glands were most commonly affected just as they are in cervical carcinoma. The glands were involved, although the parametrium was perfectly free in several of his cases. As a result of his study, he believes that the chief channels for metastases in cancer of the uterine body run: (1) along the upper edge of the broad ligament to the ovary, then along the ovarian vessel to the common iliacs and the aorta, and thence to the lumbar glands; (2) from the middle of the

corpus uteri, transversely through the broad ligaments to the iliac glands at the bifurcation of the common iliac artery; and (3) along the walls of the tubes.

Others have found rather similar percentages of glandular involvement. Baisch found the glands involved in 4 of 24 cases, of which 3 showed involvement of the peritoneum and 1 of the parametrium. Meyer, who reviewed Doederlein's material from 1902 to 1905, found the glands involved 4 times in 28 cases which were treated by abdominal operation. Offergeld found the iliac and inguinal glands involved in 2 of 15 cases, although each presented a small primary tumor. Von Herff has made similar observations. Cullen found cancerous glands only in a single case.

Nearly all agree that the parametria are not involved until fairly late in the disease. Kundrat found parametric invasion in 55 per cent of his cases of cervical carcinoma, yet in cancers of the body it was free in nearly all save the very late cases. Yet the parametria have not been subjected to the same careful study that has been made in cancers of the cervix. Baisch studied the parametrium in 24 cancers of the uterine body and found cancer but once. Pankow studied the parametrium in 3 cases, all of which were free. Weibel studied 9 cases; the parametria were free in 7, although the glands were involved in 2 of these. One of the 2 cases in which the parametrium contained carcinoma had glandular involvement as well. These findings must be taken into consideration in determining the type of operative treatment.

Late in the disease, the cervix may be invaded rarely by direct extension through the internal os, or more commonly by lymphatic metastases. We have already called attention to the fact that the lymphatic plexus in the uterine body and cervix is continuous without any clear line of demarcation. The vagina may also be invaded by metastatic extension; very rarely, it is involved by direct extension through the cervical canal.

The ovaries are often affected. They may be involved by direct extension through the uterine wall to the peritoneum and along the ovarian ligament, or by lymphatic metastases. The cancerous areas are often small and found only after careful examination. Occasionally, the ovarian metastases are of considerable size and may be larger even than the primary uterine growth. The fallopian tubes may be invaded in a similar manner.

Metastases in remote organs are relatively rare. They are mentioned in the discussion of uterine carcinoma in general (see page 203).

Complications.—Fibroid tumors often coexist with cancer of the endometrium, in marked contrast to cancer of the cervix. Many have

urged that the frequent occurrence of fibroids and adenocarcinomata of the uterine body suggests a common etiologic factor. They state that the circulatory disturbances may well account for the condition which is often found in an endometrium which has diminished resistance because of the changes induced by the fibroid. Clinically, the frequent association of carcinoma of the uterine body with fibroids should be borne in mind, since the symptoms of both conditions may be identical and the presence of the carcinoma may not be suspected. The importance of sanguineous discharges after the menopause in a fibroid uterus cannot be emphasized sufficiently.

Multiple Cancers.—The association of two or more malignant tumors is occasionally noted. The disease is often found together with cancer of the cervix, or cancers of the ovary. Cancer of the uterine body may also occur with mammary cancer and primary carcinoma of the intestines. Outerbridge has collected 27 cases of combined carcinoma and sarcoma of the uterus.

Pyometra.—Pyometra may occur together with carcinoma of the uterine body. The mechanism of the retention appears to vary in different cases; sometimes the discharges are retained by an obstruction in the lower part of the organ; in other cases, they may be withheld because the uterine wall is not able to expel them, because of atrophy associated with senility or, because the wall has been weakened by ulceration of its surfaces.

Symptoms.—Symptoms are usually present for a considerable period before the patient seeks medical advice. In spite of this fact, the prognosis is favorable in comparison with that of carcinoma of the cervix because the onset is not so insidious and the disease remains localized for a fairly long time.

The symptoms are identical with those of cancer of the cervix. The chief difference is that leukorrhea is not noted as a rule as long before the appearance of blood as in carcinoma of the cervix. Hemorrhage comes early and for a long time is apt to be only spotting. Sudden hemorrhages are not likely to come without previous warning. Pain is a late symptom. The malodorous discharge carries no especial significance, since it depends upon changes in the vagina.

Diagnosis.—The diagnosis of cancer of the body of the uterus is usually made with the microscope, since there are no characteristic symptoms or findings in the earlier stages of the disease. It is often made in the laboratory upon growths which were removed under the impression that the condition was only a fibroid. There are many cases in the literature which were considered only retroversions of the uterus and were treated by suspension after a preliminary curettage. The diagnosis in these cases was made by the routine examination of the

scrapings some days after the operation. The need for routine laboratory examinations of all scrapings is perfectly obvious.

Just as in carcinoma of the cervix, we should regard any case as cancer which presents leukorrhea and bleeding until the tentative diagnosis has been disproved by careful microscopic study. All scrapings should be studied macroscopically before they are sent to the laboratory. White, opaque fragments removed by the curette usually indicate a cancer of the endometrium, yet in early localized cases, a small focus may be missed and the diagnosis can be made only when many blocks of the scrapings have been examined. The need for a close association of laboratory and operating room cannot be advocated too strongly. Modern methods demand that all tissues removed in the operating room be studied immediately by frozen sections so that there may be no chance that a diagnosis of malignancy be made only long after the completion of the operation.

If the curetings contain malignant areas, the glandlike spaces are usually increased greatly in number so that they often lie close to each other, with only a fine dividing line of spindle cells between them. The acini frequently show marked irregularities in outline, and may form an intricate network in which it is impossible to distinguish the individual gland. The characteristic findings are an increase in the number of layers and cells lining the glands, irregularities in the size of the individual cells and their nuclei, evidences of mitosis and of invasion of the stroma by the proliferating cell. Care must be taken to distinguish from cancer, a normal gland which has been cut obliquely in thick sections. The lining of the gland in malignant adenoma is often a single layer of high cylindrical cells, the nuclei of which are irregular in shape and size, and are placed at uneven levels. Groups of cells projecting in the lumen of the gland, staining irregularly, and presenting mitotic figures are suspicious of malignancy and necessitate a careful routine study of the entire mass of scrapings. When the diagnosis is made by the immediate examination of the scrapings, the case should at once be prepared for the removal of the uterus.

Treatment.—The treatment is operative, which nearly all agree gives better results than radium. There is not yet unanimity of opinion as to the extent of the removal, provided that panhysterectomy with removal of the adnexa is the minimum. The student should realize that cancer of the uterine body is a comparatively rare condition and that there are few large series of results from which we can make deductions.

There is no doubt that vaginal hysterectomy has cured many cases in which the disease was not far advanced, although all agree that it is not the method of choice, since the upper limits of the growth must remain unknown. The results are shown in the following table:

Vaginal hysterectomy	Number of cases	Per cent of five-year cures
Glockner, 1887-1897.....	6	66.7
Krukenberg.....	6	66.7
Reipen.....	8	75
Fränkel.....	30	60
Chrobak, 1900.....	8	75
Winter, 1900.....	30	53.3
Blau, 1903.....	17	76.4
Zurhelle, 1905.....	33	60
Aulhorn, 1909.....	9	77
Egli, 1918.....	13	92

Little can be judged concerning the primary mortality, since the great majority of these cases were operated a decade or more ago. Glockner had 16 per cent primary mortality; Fränkel, 5.3 per cent; Zurhelle reports 10 per cent in 42 cases in the Bonn Clinic; Aulhorn, one death in 17 vaginal cases (6.2 per cent). Rouffart, writing in 1909, stated that the average mortality for the cases so treated appeared to be in the neighborhood of 10 per cent. It is generally conceded that, in America, this operation is usually done with about 5 per cent mortality. Much better results cannot be expected because of infected vaginæ.

The results of abdominal panhysterectomies found in the literature do not appear at first sight better than those cited for the vaginal operation. Yet it appears that the abdominal operation was usually reserved for more extensive cases which could not be approached as safely by the vaginal route. Scheib reports 6 cases with 75 per cent of five-year cures; Meyer presents Doederlein's results in 26 cases, as 54 per cent of cures. Wilson groups his cases which were operated by either the vaginal or abdominal hysterectomy. There were 31 of these which had been studied for the five-year period. The primary mortality was 6.4 per cent. Twelve patients were free from recurrence at the end of five years; operative cure, 42 per cent; absolute cure, 24 per cent.

All of these cases must be considered in the light of the operability of their series. Döderlein, in one year, operated 14 out of a total of 17 cases (82 per cent operability); Zurhelle reports the same operability in the Bonn Clinic; Krukenberg operated 63 per cent of 57 cases; Olshausen had 67 per cent; Pfannenstiel, 61 per cent; Kuestner, 55 per cent; Hofmeier, 70 per cent; Aulhorn, 100 per cent.

Many careful students have called attention to the fact that cancer of the uterine body has not been studied nearly as critically as cancer of the uterine cervix. They agree that the glands are involved in a much greater percentage of cases than was formerly believed. They call attention to the fact that the cures reported by many older

observers were more apparent than real, since they were not always considered in the light of operability. Wertheim and Reuben Peterson are convinced that their results from the truly radical abdominal operation emphasize its advantages. This is well shown by Weibel's report of Wertheim's cases.

Weibel, in 1913, states that there were only 70 cases of carcinoma of the uterine body seen during fourteen years in Wertheim's clinic, although more than 1,500 cases of carcinoma of the cervix presented for treatment during the same period. Of the 70 cases, 97 per cent were operable, although only 67 cases were actually operated. Vaginal extirpations were done 36 times in the earlier years with 1 death. Simple abdominal panhysterectomy was done 12 times with 2 deaths. Supravaginal amputation was done 3 times without death (condition probably not recognized at operation). The radical abdominal operation was done on 16 patients, 4 of which died. The mortality for the entire series was 10.5 per cent. Weibel states that this was due to the large number of elderly women in the series, and their poor condition. His series contained a number of complications. In the 67 operative cases, there occurred, in addition to cancer of the corpus, fibroids in 19 cases; ovarian cysts in 5; ovarian carcinoma in 4; tubal carcinoma in 1; ovarian sarcoma in 1. The uterine carcinoma was found accidentally in 10 cases after the uterus was removed for 1 of the above conditions. Recurrence was observed in 19 cases (30 per cent) of the 60 cases which survived operation. The recurrence presented almost invariably within the first year after operation. In 2 cases, it was not due to the uterine carcinoma but to the malignant condition of the adnexa (one ovarian sarcoma and one primary ovarian carcinoma). Forty-three cases were operated more than five years prior to the time of his report. Of these, 5 died from the operation, 16 had recurrences, and the remaining 22 are alive and well for more than five years now, an operative cure of 51 per cent and an absolute cure of 50 per cent. A detailed review of the series showed that the best results were obtained by the radical abdominal method in which 71 per cent of the cases were cured (Winter's postulates) in contrast to 59 per cent of cures for vaginal hysterectomies and 43 per cent for the abdominal panhysterectomies.

Peterson, in 1916, reports similar findings. He states that, in spite of the high primary mortality of the truly radical hysterectomy, the results are better than those of the ordinary methods. Since 1912, he has had 14 ordinary hysterectomies for cancer of the fundus which showed worse primary and end results than the 11 cases which were treated by a truly radical operation.

A critical review of the literature will convince nearly any student that the question of the treatment of carcinoma of the uterine body is

passing through the same stages as has been noted in that of cancers of the uterine cervix.

Radium.—There are no series of size sufficient to permit the valuation of radium in the treatment of this type of growth. Individual experience and study of the literature shows that the tumor may be cured by operation. The majority agree with Clark that "our attitude toward cervical and fundal carcinoma is diametrically opposite. In border-line cases of cancer of the cervix we invariably employ radium. In advanced cases of cancer of the fundus, we invariably perform hysterectomy."

SARCOMA OF THE UTERUS

Sarcoma of the uterus is usually primary but may develop in a uterine fibroma; or, secondarily, from an extension of sarcoma in some neighboring structure, more commonly, in one of the ovaries. The tumor may consist of an everting fungoid growth or an inverting and infiltrating mass, and usually presents a uniform homogeneous structure quite dissimilar to the gross picture of a carcinoma.

Frequency.—Sarcoma of the uterus is usually regarded as a very rare tumor. Many authors state that it is the most uncommon of all uterine growths, yet it is more than possible that a careful microscopic examination made on all fibroids would show that the figures stated in the literature are too low to represent the frequency of the disease. This is strongly suggested by the work of Winter who found, in 1907, sarcomatous changes in 3.2 per cent of 500 fibroid cases in which only the suspicious areas of the tumor were studied microscopically while sarcoma was found in 4.3 per cent of 253 cases in which careful microscopic examinations were made as a routine. It is certain, however, that sarcoma of the uterus has rarely been reported in the literature. The earlier literature did not recognize it, but contained many instances of recurrent fibroids, which were considered as benign tumors which followed operation. Probably a considerable proportion of these were sarcoma. The first sarcoma of the uterus definitely recorded as such and supported by microscopic examination was reported by Lebert, in 1845. Yet this aroused very little interest and the subject did not attract attention until after the discussion attending Mayer's case which was reported to the Obstetrical Society of Berlin in 1860. Five years later, Virchow definitely established the condition as a pathological entity and gave the first description of a sarcoma of the endometrium. In 1867, Veit collected 3 cases of uterine sarcoma and, in 1871, Senn and Keegar reviewed the subject from a study of 9 recorded cases. Gurlt found only 2 sarcoma in 2,649 uterine tumors and remarked the frequency of carcinoma of the uterus to sarcoma as 1

to 785. Roger Williams, in his review, found only 8 sarcoma in 4,115 uterine tumors. In 1894, Whitridge Williams was able to collect but 144 cases from the medical literature. Since then, a total of about 500 cases has been reported.

The relative frequency of cancer and sarcoma of the uterus is variously given. Geisler, basing his conclusions on his Breslau material, states that the relative frequency of sarcoma to carcinoma is 1 to 50. Veit, reviewing his work in Halle for seventeen years, found 40 sarcomata in contrast to 1,493 carcinomata, a frequency of 1 to 37. Krukenberg reports that the frequency in the Frauenklinik was 1 to 47.5. Von Franqué observed the relative proportion as 1 to 20, and considers sarcoma as equal in frequency to carcinoma of the body of the uterus. Poschmann, in Halle, found that sarcomata were observed in but 16 of 403 uterine tumors, the other 387 being carcinomata. Of the 16 sarcomata, 11 were fundal and 5 were in the cervix, while of the 387 carcinomata, 10 were of the fundus and 377 were in the cervix. The proportions stated above may be too conservative, because there are many difficulties in diagnosing a uterine sarcoma. Not infrequently, the tumors may be confounded with carcinoma, since there are types of sarcoma, occurring especially in the cervix, which present an alvéolar arrangement which may be readily mistaken for a tumor arising from epithelial elements; the clinical symptoms may be identical.

Etiology.—Nothing is known concerning the etiology of sarcoma. Predisposing causes, such as heredity, previous inflammation of the uterus, obstetrical or operative trauma, previous pregnancies, apparently have no contributing relationship. Many theories have been advanced to explain the pathogenesis, but they may be grouped under the following three heads: (1) sarcomata developed by proliferation of cells of the vessel walls; (2) sarcomata developed by proliferation of the cells of the intermuscular fibrous tissue; or (3) sarcomata developed by the transformation of smooth muscle fibers. It would appear possible that each of these theories may explain the origin of certain cases, yet it is also evident that all cases cannot be explained by one theory. Virchow's theory that the tumor arises by multiplication of the cells of the interstitial connective tissue has been supported by the facts observed in a number of cases. Kleinschmidt and Pilliet and others have adduced evidence in favor of the vascular origin. Williams, Piquand, von Kahlden, Ribbert, and others, offer evidence in favor of the transformation of muscle fibers into malignant cells. Certain authors—as, for example, Ribbert—limit the term "sarcoma" to the tumors which arise by the proliferation of ordinary connective tissue, and describe the growths which develop by the proliferation of muscle fibers as a distinct variety of tumor which they designate "*leiomyoma malin.*" Ribbert believes that the latter tumor is not a degeneration of muscle cells, but the result of a proliferation of muscle fibers. In a

case described by Pavoit and Bérard, both the primary tumor and the metastatic nodules were composed of proliferating muscle.

Age.—The disease may develop in the uterus at any time from early infancy to old age; yet, as in carcinoma of the uterus, it occurs more commonly about the time of the menopause. Gusserow collected 73 cases, 4 of which were under twenty-nine years; 15, between thirty and forty; 28, between forty and fifty; 18, between fifty and sixty; and 3, in women over sixty. Meyer found that 85 cases occurred between forty-five and fifty years in his compilation of more than 460 cases. There is on record a case in which sarcoma of the uterus was observed in a woman more than seventy. Grapelike sarcoma of the cervix is slightly more frequent in infancy. Hollander reported a case in an infant of seven months.

Location of the Tumor.—The sarcoma may occur in the uterine body or in the cervix. The former position is more common. Piquand, in a study of 393 recorded cases, found that 325 were in the body and 68 were in the cervix. Other writers state that sarcoma of the uterine body are even more frequent than shown by these figures and that they occur at least five times as commonly as sarcoma of the cervix.

Classification.—Uterine sarcoma may be primary or secondary to other growths. They may also be classified according as they develop in the cervix or the body of the uterus. Each of these general groupings may be subdivided according as they develop from the mucosa or the parenchyma. The tumors may be diffuse or circumscribed. Sarcoma of the cervix may be further divided according to their morphology into two groups: (1) an indefinite group comprising the ordinary varieties of sarcoma; and (2) the mixed forms, which may contain various tissues, such as bone cartilage, etc.

(1) **SARCOMA OF THE UTERINE BODY ARISING FROM THE MUCOSA.**—This may occur in one of two forms, diffuse or circumscribed. In all probability, the type arising from the endometrium is much less frequent than that developing from the uterine wall, although it is often impossible to determine the exact point of origin of the tumor, since the growths have usually overrun all landmarks when the case first presents for treatment.

(a) *Diffuse Type.*—The diffuse type of growth is far more common than the circumscribed. It usually originates in the fundus and spreads so as to involve the whole mucosa of the uterine body. It is usually limited by the internal os, but occasionally overcomes this barrier and spreads into the cervix. These cases are usually found in the adults and are rare in early life. As the tumor grows, the uterus becomes uniformly enlarged and may resemble a gravid organ. On section, the endometrium is thickened, and presents a shaggy polypoid picture. The sarcomatous structures are homogeneous, cheesy, and pale yellow in color, although areas of hemorrhage and necrosis are often noted.

The line of demarcation between the mucosa and the underlying myometrium is usually sharp, although it is less distinct in the rapidly growing tumors which tend to spread through all the tissues. Even though gross invasion of the muscle cannot be seen with the naked eye, it can usually be made out with a microscope. The tumor may extend along the fallopian tubes or directly through the uterine wall.

(b) *Circumscribed Type*.—This begins as a nodule in the deeper part of the endometrium and may extend inward into the uterine cavity or outward into the uterine wall. In the former case, it develops in the cavity of the uterus and presents as a fibroid polyp. This tumor may finally dilate the cervix and reach into the vagina when portions may slough off and be expelled or the whole mass may become strangulated and secondarily infected. When it grows outward, it may perforate the uterine wall and invade the peritoneum of Douglas's pouch or may grow into the cornua of the tubes. Histologically, these tumors may present any variety of a sarcomatous cell, although the round-celled type seems more common. Blood vessels are numerous and enlarged sinuses are frequently found. The sarcoma cells often present a distinct perivascular arrangement. The supporting stroma varies greatly in amount but usually is scanty. When the uterine wall has been invaded, necrosis commonly ensues. Secondary infection and hemorrhage is common. Pigment is often found in the cells of cases which are complicated by hematometra or pyometra. Melanotic uterine sarcomata have been reported. The pelvic lymph glands which are involved may present cystic degeneration.

(2) SARCOMA OF THE UTERINE MUSCLE.—This tumor may arise as a primary growth, or may develop in a preëxisting fibroid. It may likewise appear in one of two forms: (a) diffuse; or (b) circumscribed.

(a) *Primary Diffuse Type*.—This type is very rare and is not often considered in pathological descriptions. When the uterus is involved by this growth, usually it becomes soft, smooth in outline, and resembles a pregnant organ. The cavity is usually enlarged and the endometrium is thickened. The tumor may invade the mucosa and project into the cavity of the uterus when it is only with the greatest difficulty distinguished from a primary growth of the endometrium. Histologically, the growth is composed of round or spindle-shaped cells found diffused throughout the entire thickness of the uterine wall, lying between what is left of the muscle fibers. The tumor cells are believed to originate from the intermuscular or perivascular connective tissue. It is quite possible that many of this class of tumors are better described as peritheliomata.

(b) *Primary Circumscribed Type*.—This type consists only of sarcomatous nodules which arise *de novo* in the uterine wall. It is highly probable that many cases are confused with sarcoma arising in a fibroid which is more common. It is agreed, however, that these two forms

account for the great majority of uterine sarcoma. In the earliest stages, the growth is definitely circumscribed, although it is rarely encapsulated. Microscopically, the very early stages may be indistinguishable from early fibroids. Later, it spreads and invades the uterine wall and becomes either subperitoneal or submucous. The former type may break through into the pouch of Douglas. The latter projects into the uterine cavity and tends to become polypoid. It may project through the cervix and resemble the grapelike sarcoma of the cervix (Pick). Obviously, these cases may be confused with growths which originate in the endometrium.

The entire group of polypoid cases may be confused with "recurrent fibroids." Under the latter term are designated tumors which successively cast off pedunculated masses from the uterine cavity, which are considered fibroids until their true nature has been disclosed by histologic study after removal of the uterus. Thus Holland records a case in which three fibrous polypi were, within a few months, thrown off spontaneously from the uterine cavity or were removed by the snare. There were no histologic examinations. When the uterus was subsequently removed, it was found to contain a large sarcoma which, originally circumscribed, was rapidly becoming diffuse. Croom records a similar case which, in his early experience, returned to his wards in Edinburgh six times in a little more than two years. On each occasion, he removed, by a snare, huge masses of apparently edematous fibroids, some of which were as large as a fetal head. The pathologists considered them fibroids. When the uterus was finally removed, it was found to be sarcomatous. Such cases may, however, represent the large class of cases in which the fibroids secondarily become sarcoma.

The sarcomata which remain localized in the uterine wall seldom attain any great size. On the contrary, the submucous and subserous forms may attain enormous dimensions. Perrin described a case weighing nine kilograms while Piquand's case weighed twenty kilograms.

The consistency of the tumors varies, since they frequently contain cysts. They are never as hard as fibroids. On section, they present a homogeneous, cheesy or brainlike appearance and are yellowish-pink in color. They frequently show areas of old hemorrhages resulting from rupture of the thin-walled capillaries. Cysts are common and may be as large as an orange. The smaller ones result from edema, while the larger ones result from lymphatic dilatation or from necrosis of the sarcomatous tissue. There are also telangiectatic varieties, which contain many large sinuses composed of dilated blood vessels. Histologically, the tumors are found to contain both round and spindle cells, although pure forms are recognized. The presence of giant cells should excite the suspicion that the tumor is a rhabdomyosarcoma.

(3) SARCOMA ARISING FROM A PREEXISTING FIBROID.—This type usu-

ally arises in the center of the fibroid and presents an area which may be clearly differentiated from the surrounding fibroid tissue. Occasionally, it is found in the periphery of the tumor. While fibroids rarely occur singly, the malignant change is usually found in only one of the group. The condition is readily recognized in developed cases, although the early stages may not show macroscopic change. The tumor may be somewhat circumscribed or occur as a diffuse infiltration throughout the fibroid tumor. With the advance of the growth, metastases may appear in the muscular wall of the uterus outside of the fibroid proper. On cut section, the sarcomatous area presents the usual homogeneous, cheesy, yellowish appearance with frequent hemorrhagic areas and cystic spaces.

The *histogenesis* of this type of sarcoma has been the subject of much discussion and various theories have been advanced to explain its origin. All agree that sarcoma may develop from the connective tissue of the fibroid. There is a difference of opinion as to whether it may also arise from muscle cells. Von Kahlden was the first to claim to have observed the direct transition of the myomatous cells into sarcoma cells. While all have not accepted his case as proved, there is no doubt concerning Williams' case and that of a long list of others. Kelly and Cullen observed the transition in 13 of 17 cases and Meyer states that the muscle cell sarcoma is the most common form of uterine sarcoma. The majority of the men who are interested in this phase of the subject regard the transition from muscle to sarcoma cells as an instance of metaplasia from a muscle to a connective tissue type of cell. Meyer, on the other hand, does not agree, and believes that the tumor is but an instance of a destructive, exuberant growth of immature muscle cells, the degenerate forms of which are indistinguishable from those of connective tissue cells. The transition usually appears as a gradual enlargement of the ordinary fibromyomatous muscle cell and of its nucleus, with an increase in the nuclear chromatin until there presents the large spindle-shaped sarcoma cell. The change can be seen usually only in the periphery of the fibroid nodule.

The differentiation between rapidly growing fibroids and a definite malignant neoplasm may not be easy. What one observer would regard as benign may be classed as malignant by another equally competent pathologist. There is, however, some prospect of attaining more definite knowledge as a result of Mallory's stains, by which special method he has been able to demonstrate the different features of the myoglia and the fibroglia fibroids. Naturally, the confusion in the differentiation obtains only in the tumors which have not given metastases.

SARCOMA OF THE CERVIX.—(a) ARISING FROM THE MUCOSA.—This may occur as: (1) diffuse; or (2) circumscribed growths. Of special interest is that form of circumscribed cervical growth which has been

designated as grapelike sarcoma of the cervix or sarcoma botryoids. This tumor arises from the superficial layers, either of the mucosa of the cervical canal or from the portio, and comes to assume an appearance not unlike that of a bunch of grapes or of a hydatidiform mole. It usually grows very rapidly and may completely block the canal, protrude from the cervical os, and even fill the vagina. It may appear at any age. The tumor begins as small polypoid outgrowths which cannot be distinguished from a simple mucous polyp by the naked eye. In the beginning, the growth develops slowly but, after a variable period of quiescence, it rapidly enlarges. The tumor is composed of two distinct portions, a superficial part containing the translucent vesicles, and a supporting stem of fibrous tissue which is continuous with the submucosa of the cervix. As the disease progresses, the vaginal vault is invaded and finally the mucosa is penetrated and the neoplasm infiltrates the vesicovaginal and rectovaginal septum, and ultimately the parametric and regional lymph glands become involved. Distant metastases have been described, although rarely. On microscopic examination, the growth is found to correspond to that of myosarcoma of the vagina. The free surface of the vegetations are covered in part by typical epithelium of the cervical canal, and the remainder by cells derived from the stratified epithelium of the portio. There is usually considerable superficial erosion. Striated muscle and hyaline cartilage have been found in the deeper portion of the neoplasm. Webber first reported the general type in 1867, although the subject did not assume interest until following Spiegelberg's paper in 1879. The term "grapelike" was suggested by Pfannenstiel in 1892, although it was not then recognized that the cystic spaces in the tumor were due to edema from the rapidly growing sarcoma.

(b) ARISING FROM THE FIBROMUSCULAR COAT OF THE CERVIX.—This form is very rare. It may arise as a primary growth or as a malignant degeneration of a preëxisting fibroid. The latter are at first circumscribed but may break through and present upon the surface as a more diffuse growth. In the diffuse form, the mucosa may be entirely involved but usually the vaginal portion of the cervix shows the most extensive invasion. The cervix appears greatly hypertrophied and infiltrated and its surface may be covered with irregular vegetations which resemble very closely carcinoma. The circumscribed type may be either sessile or pedunculated, the former appearing as an irregular vegetating growth which arises from either the anterior or posterior lip. Piquand states that this form may be differentiated from a carcinoma by its greater softness and size. There is also less tendency to necrosis.

The pedunculated sarcoma or sarcomatous polyp is the most common form of cervical sarcoma. It may be attached to the cervical canal by a pedicle of various lengths and thicknesses, or to the vaginal

portion of the cervix when it appears as an irregularly rounded tumor which is sometimes lobulated. It is soft in consistency and pinkish gray in color. Occasionally it is fairly dense, when it is composed of cellular tissue without evident edema. The early growth has a smooth surface, covered by normal epithelium which later becomes eroded. Extensive degenerations are not uncommon.

Round-, spindle-, and mixed-cell sarcomata occur with about equal frequency. Giant cell growths are also described. There are records of several melanotic sarcomata, one of which, quoted by Williams, had given pigmented metastases to the brain and other organs. Girandel described a case in which myomatous nodules were found in the liver, kidney, intestines and uterus, and which contained melanotic cells. Hyaline degeneration is frequently found, particularly around blood vessels and in the older portions of the tumor.

Special Forms and Mixed Types.—A large number of sarcomata must be placed in this group. Their interest is chiefly from the pathologic side. We have already mentioned melanosarcomata. Many would place myxosarcomata under this classification, although Piquand believes that the majority of these are really edematous tumors. Von Franqué, and a few others, however, have recorded true myxomatous tumors. Lymphosarcomata have been described by Gow, Schlagenhauer, and others. They were characterized by a rich lymphatic plexus with numerous dilated spaces which accounted for the softness of the tumor.

A lipomyosarcoma has been described by Sitzenfrey.

True angiosarcomata have been reported in which the tumors were partly composed of sarcoma cells and partly of new-formed blood vessels. Often, however, we find a perivascular arrangement made by the sarcoma cells, while the blood vessels have not developed to an extent which warrants the term "angioma." Some of the peritheliomata are described as alveolar sarcomata.

A number of cases have been described in which cartilage was present in the sarcomatous mass. This type is termed chondrosarcoma. Some believe that the cartilaginous areas are due to a metaplasia of the connective tissue cells; the greater number, however, regard the growth as a mixed mesodermal tumor. Cartilaginous elements have been observed in the grapelike tumors of the cervix by Pfannenstiel, Pernice, and others. An adenofibromyxochondrosarcoma of the cervix has been described by Puech and Massabuau.

Rhabdomyosarcomata have been reported by a number of authors. Bell has collected 17 such cases. The majority of these mixed types occur in the cervix. Herb states that only 8 have been found in the body of the uterus, for the most part in the cornua or on the posterior wall.

There is a confusing group of tumors which are usually termed car-

cinoma sarcomatodes, which appear to present both the characteristics of carcinoma and sarcoma in a single specimen. Formerly they were regarded as a separate type, but, in recent times, the majority of students consider that they are properly sarcoma. Some have been reported as endothelioma, presenting an alveolar arrangement which is most difficult to distinguish from carcinoma but have been excluded in the critical studies by the students of endothelioma. There are, however, a number of cases which have been adduced by competent men as examples of double malignant tumors. Fisher-Defoy and Lubarsch, in 1905, admitted that there were 13 cases entitled to this classification. Taylor and Teacher, in 1909, recorded 6 others, 4 of which occurred in the body of the uterus. Johnstone states that this group is of particular interest in the light of Russell's demonstration that sarcoma may develop during the experimental propagation of an adenocarcinoma of the mouse.

Method of Extension.—Uterine sarcomata are spread by direct extension and by metastases. In the earlier stages, the growth may be definitely circumscribed, but, in its development, the tumor spreads outward toward the peritoneal cavity or inward toward the uterine cavity. Cervical sarcomata spread toward the vagina. Uterine sarcomata often remain dormant or grow slowly for a long period and then develop very rapidly. This feature of growth is seen especially in the cases in which sarcoma originates in the fibromyomatous nodules and may be accounted for by the resistance of the capsule.

The later stages are usually accompanied by metastases. Masses may be found in the posterior cul-de-sac, or the parametrium, which may be so filled with malignant tissue as to exert pressure on the ureters and cause hydronephrosis. This complication, however, is not as frequent as in carcinoma. This type of invasion has been adduced as an example of metastases, yet is probably due to direct extension. Metastatic deposits may be found in remote organs, as the lungs, liver, and retroperitoneal glands. The cells are carried by the blood channels, and Katz has found sarcomatous emboli in the pulmonary veins. Sarcomatous thrombi are often found in pelvic veins. The extension may also occur through the lymphatics, as is proved by cases presenting discontinuous involvement of the parametrium. Gessner believes that metastases are more frequent than is usually considered, and can be proved only by careful post-mortem examination. The frequency of recurrence after operation certainly supports this view.

Complications.—Pyometra and hematometra may occur when the drainage of the uterus is blocked by the tumor. Occasionally, the uterine cavity may be distended with a large amount of fluid. Terrillon reports a case in which the uterus contained seven liters of fluid and refers to a case of Pean in which there were fifteen liters. There are a number of cases of inversion of the uterus cited in the literature. These

have occurred almost without exception when the sarcomatous mass was of considerable size. The peritoneal cavity has been opened in several cases when the physician mistook the inverted fundus for the pedicle of the tumor. There are at least 2 cases in which the inversion occurred in nulliparous women (Simpson, Spiegelberg). Constitutional symptoms may be caused by secondary changes in the tumor, such as necrosis and hemorrhage.

Symptoms.—The classical symptoms are hemorrhage, pain, discharge, and pressure. The extent and intensity of these vary greatly, depending for the most part upon the size and situation of the tumor. Very rarely, cachexia is the first symptom, noted almost without exception when the growth has developed in the vaginal fornix and has grown in the plane of least resistance down into the vaginal cavity.

The hemorrhage usually first appears as a prolonged menstrual period. It may not occur, however, until after the menopause. Irregular hemorrhage may occur after over exertion or trauma. Since the growth does not ulcerate as a rule as early as carcinoma, the hemorrhage usually comes from hyperemia of the mucosa.

Pain is a common symptom. Its amount varies, depending upon the location of the tumor. It may be very intense when the uterine cavity is suddenly distended as by polypoid growths or hemorrhage. There is much pain in the late stages of the disease as a rule. There are a few cases in which tumors of considerable size were not accompanied by pain. Clay, A. R. Simpson, Howard Taylor, and others have reported examples. There may be very little pain when the sarcoma has developed in fibromyomatous nodules and has not broken through the capsule.

Discharge is usually present in the intervals between the hemorrhages. It resembles ricewater in appearance and is not often as offensive as that in carcinoma. When the disease has progressed to a considerable extent, the discharge may be very fetid. The older writers call attention to the presence in the discharge of grayish white shreds, resembling particles of brain matter. These are tumor masses which have broken away. They are diagnostic when they occur, but since they occur late in the disease, the diagnosis should already have been made.

The symptoms vary somewhat, depending on the location of the tumor.

Sarcoma of the Uterine Wall.—The symptoms of this type of growth may be that of an ordinary fibroid unless it develops after the menopause. The hemorrhage usually begins as a menorrhagia. The anemia, however, is more marked than that of fibroids in general. The development of cachexia may first reveal the true nature of the tumor. In the interval between the hemorrhages, there is present, in the later stages of the disease, the watery discharge which has just

been commented upon. If the tumor grows toward the peritoneum, there may be only slight menorrhagia as an early symptom. There is usually not much pain with interstitial tumors. It is more common with the subperitoneal growths which are complicated by peritonitic reactions. The pain may be intense as a result of the spasmodic contractions of the uterus in its efforts to expel submucous tumors.

Sarcoma of the Endometrium.—The symptoms of this group are similar to those of uterine cancer, namely, hemorrhage, a watery discharge which finally becomes purulent, and pain. The bleeding soon becomes continuous. Pain is usually a late symptom. It is severe, when the growth has become pedunculated and causes spasmodic contractions of the uterus, or when the tumor has penetrated the parametrium. It is a common sequence of secondary infection.

Sarcoma of the Cervix.—Many of these cases give no symptoms until very late in the disease, especially if there is no necrosis of the tumor. As a rule, however, the hemorrhage is profuse, as is the watery discharge, and anemia develops at a fairly early period. Pressure symptoms are almost invariable when the tumor is large and fills the vagina, since the pelvic organs are usually infiltrated by sarcomatous cells and secondary infiltration.

Diagnosis.—Correct diagnosis is fairly uncommon until late in the disease, since the symptoms at first resemble those of an ordinary fibroid. Rapid enlargement of a uterus which is known to contain a fibroid should excite suspicion, although this feature often follows degenerations in a fibroid tumor. Sarcoma should be suspected when the tumor increases after the menopause or when hemorrhage recurs after the climacteric has been definitely established. The presence of ascites should also suggest the diagnosis, although this symptom may be seen in connection with nonmalignant tumors.

If the tumor projects through the cervix, the mass will be found soft and pliable and composed of polypoid masses. Irregularities in the uterine cavity may be felt if the cervix is open sufficiently to admit the finger. The diagnosis may be made from uterine scrapings in the majority of cases, although there are many sarcomata which have not yet involved the endometrium when the case presents for treatment. Unfortunately, the diagnosis is usually made only after removal of the uterus.

Prognosis.—The prognosis of uterine sarcoma is extremely grave when the tumor is of the rapidly growing type. Yet, as in sarcoma of other organs, it varies somewhat according to the histogenesis of the tumor. Thus, the fibrosarcomata occasionally grow so slowly that there may be many years before the fatal issue. Gusserow described a case of more than ten years' duration. The average duration is usually placed at three years, but cases may earlier come to fatal issue. The question is confused because many cases develop in fibroids and it

is difficult to tell when the sarcoma begins. The round-cell forms are more malignant, as a rule, than the other types. The giant-cell tumor is the least malignant. Grapelike sarcoma is very malignant.

Treatment.—Radical removal of the uterus and appendages is imperative in the presence of a tumor in which the condition is suspected. This suffices, as a rule, for sarcomata which have developed and are still local in the uterine wall. Other types of the tumor should be treated by the abdominal radical method described for cervical carcinoma. The results, unfortunately, are not good. There are comparatively few cases of simple hysterectomy which have not been followed by recurrence. Radium treatment should give better results than incomplete operations. When recurrence takes place, it develops usually with astonishing rapidity. The great majority die within a year. Gessner reports a recurrence following a radical operation in 10 of 26 cases originating in the endometrium. Sixteen cases were cited as cured, although only 5 had been observed for five or more years. Recurrence was noted in 14 of 35 cases of sarcoma of the uterine wall. The remaining 21 were accounted as cured, although only 5 had been followed for five years.

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CHAPTER XI

CHORIO-EPITHELIOMA

Definition—Historical—Marchand's theory—Classifications—Ewing—Geist—Frequency—Etiology—Hydatidiform mole—Age—Location of growth—Period of latency following pregnancy—Metastasis—Ovarian changes—Symptoms—Diagnosis—Microscopic diagnosis—Differential diagnosis—Prognosis—Treatment—Operation—Radium.

CHORIO-EPITHELIOMA

Chorio-epithelioma is a very malignant tumor which invariably arises in connection, either immediate or remote, with a pregnancy. It develops from the chorionic villi after labor at full term, abortion, hydatidiform mole, and occasionally even before the products of gestation have been expelled from the uterus. It arises from the fetal ectoderm and is composed of varying proportions of syncytial and Langhans' cells derivatives. It is found most frequently in the uterus but has been described in the tube and ovary. These tumors attract interest because of the great variation in their malignancy, since some kill most quickly, while others are seemingly benign. The frequent lack of coördination between the clinical and pathological findings which makes it impossible to determine before the tumor has run its course as to its degree of malignancy, and the fact that there are spontaneous cures even after the development of metastases, the recognition of similar histologic appearances in teratoma, all tend to make the subject one of the most interesting and debatable chapters in pathology.

Historical.—The fact that there were malignant tumors closely allied with pregnancy and hydatidiform moles was recognized in fairly early medical literature, yet no attempt was made to classify them until quite recently. As early as 1877, Chiari described 3 cases which he considered atypical carcinoma which developed coincidentally with pregnancy. Säger, in 1889, first definitely recognized the disease as a clinical entity and classified it as a sarcoma which developed only in a gravid uterus. Believing that the decidua was the site of the neoplasm, he termed the tumor deciduoma malignum. Säger's view obtained support in 1890 by Pfeiffer, a pupil of Chiari, who met with a similar case and quite independently came to the same conclusion and gave his tumor the same name. Pestalozzi, in 1891, described 3 cases, although he could not decide as to their cellular origin. Other cases were soon reported by Schmorl, Müller, Gottschalk, and Lebensbaum, none of

whom completely accepted Sanger's views. In 1893, Sanger reviewed the subject and modified his views to some extent, although holding the conviction that the essential malignant elements of the tumor were derived from decidual cells and that the chorionic elements were merely adventitious.

Gottschalk, in 1894, first advanced the theory that the disease was primary in the fetal tissue, being essentially a sarcoma of the chorion, arising from the Langhans' layer, which was then regarded as fetal mesoblastic tissue, and from the stroma of the villi. A number of cases were reported in the same year by others without advancing new views concerning the origin of the tumor.

Considerable confusion was added to the subject because of the erroneous views which existed at that time as to the origin of the syncytium and Langhans' cells layer. The majority believed that the former was of maternal and the latter of fetal origin. No firm advocate that the syncytium was derived from fetal ectoderm had yet become intensely interested in this type of tumor. Whitridge Williams, in describing his tumor in 1895, recognized its connection with the chorionic epithelium and, although he described the importance of the Langhans' cells, he considered the syncytium as the more essential element.

Marchand's Theory.—Marchand's monograph in the same year (1895) did much to clear up the subject and to establish the pathology on the present basis. He identified the tumor cells as derivatives of both layers of the chorionic epithelium, and recognized the etiologic features contributed by hydatidiform mole. The subject appeared most confusing, since he accepted the ruling opinion as to the nature of the syncytium, and saw the tumor as of mixed maternal and fetal origin. The frequency with which hydatidiform mole precedes chorio-epithelioma had been noted by previous observers. Some had sought to establish a causal relationship between the two. Marchand, however, was the first to recognize the true pathology of hydatidiform mole as an excessive, irregular proliferation of both layers of the chorionic epithelium, together with the degeneration of the mesoblastic cores of the placental villi. The older view was that of Virchow, who saw in the mole only a myxoma of the chorion. Marchand traced a very close likeness between the hypertrophied epithelium of the mole and the cells of the chorio-epithelioma. Not only were the cell forms similar, but they infiltrated the maternal tissues and invaded the blood vessels in a similar way. The invasion appeared only as an exaggeration of the conditions found about the attachment of the villi to the decidua in the young placenta. He regarded chorio-epithelioma as a member of a series of diseased conditions of the chorionic epithelium which showed many varieties and a progression in degree of malignancy comparable with that seen in other tumors, such as the cell picture seen between

simple adenoma and malignant adenoma, and simple papilloma and carcinoma. He, however, considered it impossible in any given case to distinguish sharply between the proliferation seen in a simple hydatidiform mole and the malignant tumor.

He divided the malignant chorionic epithelioma into two classes, typical and atypical, between which were certain transitional forms.

The typical chorio-epithelioma are those in which is reproduced the character of the chorionic epithelium as it occurs in early pregnancy, either changed or with little alteration. In this type, syncytial masses are seen in the well-known form of irregular, multinucleated columns and branching protoplasmic masses, associated with more or less well-developed polyhedral cells of the Langhans' layer.

The atypical group shows invasion of the musculature of the uterus by syncytial masses or individual giant cells. It is characterized by the absence of Langhans' cells.

In the transition forms between these two types, there is an increasing proportion of syncytium and wandering cells, and decrease or absence of Langhans' cells as compared with the typical tumors. Marchand felt that the two types did not differ markedly in malignancy, although the typical group gave rise to rapid metastases through the blood stream while the atypical forms caused more local destruction.

Marchand's views gradually gained general acceptance. Nearly all authors who described cases after 1895 regarded their tumors as derivatives of the chorionic epithelium, while the observers of the older cases reexamined their tumors and retracted their former opinions. It was not until 1903, however, following Teacher's monograph, that the English school fully accepted Marchand's teaching, possibly because the English were chiefly responsible for the belief that syncytium was altered fetal ectoderm.

Attempts at Classification Based on Histologic Picture.—In spite of the great progress in the histologic knowledge of the disease, as reports of cases multiplied, it became more and more apparent that the relation between the histologic structures and the clinical prognosis was most uncertain, and that many curious features of these growths, especially the spontaneous recovery of apparently hopeless cases, were wholly unparalleled by any other malignant neoplasm. Von Velits was the first to maintain that the more benign growths presented definite histologic features, such as: (1) absence of mitosis in Langhans' cells; (2) degenerated areas in both cell derivatives; and (3) comparative or complete absence of Langhans' cells. Schmauch also emphasized the relation between the Langhans' cell derivatives and the degree of malignancy. He saw the malignant type only as a cellular infection of the organism by derivatives of chorionic epithelium. While there is wide dissemination of chorionic cells as a physiologic

process during pregnancy, the normal protective powers of the female organism prevent their proliferation. The latter phenomena is possible, therefore, only in the absence of cytolytic forces. Schmauch differed from Marchand only in that he saw that the literature indicated that nearly all cases which died of general metastases were of Marchand's group of typical chorio-epithelioma. While the transitional types might kill, the greater number gave only metastases in the lungs without generalization. He stated that not one case of generalized metastases in an atypical chorio-epithelioma had been reported. Others, as R. Meyer, and Schlagenhauser, also attempted to establish definite histologic criteria without definite results.

In 1910, Ewing made a more elaborate histologic classification than that of any previous author, attempting to separate the malignant from the semibenign tumors on the basis of histologic appearance and thus to establish a more definite criterion for treatment. He divided the typical chorio-epithelioma of Marchand into (*a*) benign chorio-adenoma; and (*b*) the very malignant choriocarcinoma.

The chorio-adenoma, previously known as malignant placental polyp, is composed of elongated hypertrophied villi, the margins of which are covered with actively proliferating cells of both types of fetal epithelium. These villi infiltrate the uterine sinuses, usually over a large area, enlarge the uterus uniformly and often project as a polypoid mass into the uterine cavity. They tend to remain long confined within the uterine cavity or wall, although occasionally they invade the broad ligament and pelvic veins and give metastases containing villi to the vagina or the lungs, but rarely, if ever, give rise to general metastases. The tumor reproduces in a rather orderly fashion all the structures of a normal villus without metaplasia or morphologic variations from the normal type of cell, although an entire villus may not necessarily be present in each individual specimen presented for examination.

The course of chorio-adenoma resembles in many respects that of the more malignant chorioma, but differs in certain essential features. It tends to produce greater enlargement of the uterus, often with polypoid tumors distending the cavity, and usually perforates that organ but slowly, and does not necessarily extend into the pelvic veins. It may be cured by curetting, or by partial removal, and perhaps by spontaneous expulsion, results not observed with more malignant tumors. Though it produces metastases, they are likely to be limited in extent and may undergo spontaneous retrogression, a feature almost unknown in choriocarcinoma.

The malignant choriocarcinoma of Ewing exhibits a very different structure. There are absence of villi, but a very extensive proliferation and pronounced metaplasia of both Langhans' cells and syncytium. The tumor cells exhibit a remarkable capacity for independent growth; in metastases,

they present a striking lack of differentiation. They grow diffusely without the orderly arrangement or polarity seen in the milder forms of chorionic tumors. The primary tumor of the uterus is comparatively small, and does not enlarge the organ, yet numerous metastases may be found in lungs, spleen, brain and other organs. As indicated by the histology, the cancer is of high potential malignancy and it is doubtful whether any cases purely of this type have recovered. Ewing admits the possibility of intermediate forms between his two types of chorio-adenoma and choriocarcinoma.

The atypical chorio-epithelioma of Marchand is divided by Ewing into two groups: (a) syncytioma; and (b) syncytial endometritis. The local uterine growth is not clearly defined in these forms as in the chorio-adenoma and choriocarcinoma. In its place, there is a bulky mass which may fill the cavity and enlarge the organ, composed of uterine stroma infiltrated with large or giant acidophil cells of the general type of syncytial wandering cells. Mingled with these is much fibrin and necrotic detritus, and the mass is swollen by exudate and hemorrhage. The size of the primary growth may vary and may be limited to a small area of the mucosa or infiltrate the entire wall. Rarely it extends through the wall into the broad ligaments. Progressive metastases have not been observed according to Ewing, but Fleischmann has described a vaginal tumor presenting the structure of these atypical chorioma which may have arisen from deported villi. This group of syncytioma probably arise as retrogressive processes from one of several antecedent factors, chiefly abortion, hydatidiform mole, or chorio-adenoma; probably choriocarcinoma never undergoes such extensive retrogressive changes. When the syncytial cells are abundant, well nourished, and form more or less compact sheets, a neoplastic quality is suggested and the term "syncytioma" may be employed. When the lesion is more diffuse and complicated by exudative and productive inflammation, it seems best designated as syncytial endometritis.

The prognosis in syncytiomata is essentially favorable, since the process advances slowly and the life of the wandering cells is short. Early warnings are given by hemorrhages and enlargement of the uterus, and progressive metastases apparently have not been observed. Yet the disease is not without danger and many cases are fatal. In Schmauch's list, 5 per cent of his fatal cases were syncytiomata. Hemorrhage, local and general infection, peritonitis, and perforation of the uterus during curetting, are the chief causes of death.

Geist is the latest author to attempt to correlate the histologic picture with the prognosis and the type of treatment indicated. He agrees with Ewing that Marchand's atypical chorio-epithelioma is essentially benign, although it may be fatal from accidental complications. He regards Ewing's syncytial endometritis as neither a true tumor nor an inflammation, but rather as an exaggeration of the normal process of invasion of the uterine muscle by syncytial cells. He believes, there-

fore, that it is more accurately designated as a syncytial hyperplasia. In Ewing's syncytioma, he sees a transition between the syncytial hyperplasia and the more advanced forms of the chorioma, and considers it the first real step of a true neoplasm. He believes that it is not a retrogressive and degenerating chorio-epithelioma in which all the Langhans' elements have disappeared, as does Ewing, but considers it a growth composed of one definite cell type. Geist does not believe that it is possible to subdivide Marchand's typical chorio-epithelioma into semibenign and malignant type in accordance with Ewing's view of chorio-adenoma and choriocarcinoma. He agrees rather with Schlagenhauser, Marchand, Aschoff, Hitschmann, and Cristofolletti that, histologically, we cannot obtain evidence sufficiently definite to be of prognostic value. He admits that cases presenting all the histologic features of malignancy, such as invasion of the musculature by large cell masses, mitotic figures in Langhans' cells, leukocytic reaction, necrosis, thrombosis, and invasion of vessels may have a perfectly benign course. On the other hand, cases which histologically appeared more benign in which there was absence of mitosis and other indications of malignancy, have progressed to fatal issue. Geist believes that there are so many transition forms between Ewing's classification of chorio-adenoma and choriocarcinoma that it is impossible to diagnose positively by histologic means a benign type, since the tissues examined may not be typical of all the phases that are present. Geist further admits, while Ewing will not, that there are cases of truly malignant choriocarcinoma which, although present with metastases, have retrogressed spontaneously or after incomplete operations. Geist's conception seems to be that of the majority of the pathologists at the present time. Whether further experience with clinical data and exact microscopic descriptions will allow us to accept Ewing's more detailed classification with its endeavor for a more accurate prognosis, remains for the future to decide.

Frequency.—Chorio-epithelioma, when first described, was considered a disease of great rarity. Case reports, however, soon multiplied so that Teacher, in 1902, was able to collect 188 well-authenticated cases. He knew, however, of many others which had not been published, since he saw the slides of numbers of unrecorded cases in Prague and Dresden, Kiel and Leipzig. The incidence of the disease varies in different countries and at different times. In the eighteen months from February, 1901, to August, 1902, 7 cases were found in the 2,700 autopsies at the General Hospital in Vienna; yet in Budapest, where the pathologists were searching for such cases for several years, not one instance was reported. Teacher pointed out that in London, with more than twice the population of Vienna, only 7 cases were recorded and very few from other parts of England. This he attributed to the rarity of post-mortem examinations in England and to the chance

that many cases were incorrectly diagnosed as retained placenta, sepsis, or sarcoma. Pollosson and Violet, in 1913, carefully tabulated the collected cases and were able to add 238 to Briquel's 217 collected cases (1903), making in all a total of 455 cases. In 1917, Vineberg added 78 more cases, including 7 of his own. Sunde, in 1919, collected 38 cases in Christinia. Since then, isolated cases only have been reported in the literature. A review of the material unreported during the period of the war may add greatly to the list.

Etiology.—Like malignant tumors in general, the true etiology is unknown. We know, however, that with few exceptions, pregnancy has preceded the growth; it is, therefore, a disease essentially of fertile women. The frequency of the disease runs parallel with the degree of fertility. Ladinski, in an analysis of 90 cases, found an average of 4.2 pregnancies. Briquel, studying 158 cases, found 33, or 21 per cent, with the second pregnancy, 31, or 20 per cent, with the third, and 74, or 47 per cent with the fourth or more. Olivier Bauregard found that, of 178 cases, 66 had borne more than five children, whereas only 22 were nullipara. Various conditions have been suggested as predisposing factors, such as diminished resistance because of too frequent pregnancies, previous inflammatory conditions of the endometrium, and defective formation of the decidua, especially in Nitabuch's fibrin layer. On the other hand, so many patients had enjoyed perfect health up to the fatal pregnancy that it seems unjustifiable to regard preceding ill health as an important factor. Yet recently, Fink felt that, in his case, as in the older case of Lindfors, a severe attack of influenza during the pregnancy may have diminished the resistance and have made it possible for the malignant elements to gain the upper hand. Yet it seems more reasonable to accept the view of a primary fetal cause that the trophoblasts have an unusual activity which permits them to retain embryonic power of growth to the end of pregnancy and often for a much longer period.

Pollosson and Violet studied the character of the pregnancy preceding the disease in 455 cases. Two hundred and three cases, or 45 per cent, followed a hydatidiform mole. One hundred and thirty-five cases, or 30 per cent, followed abortion. Ninety-nine cases, or 21 per cent, followed labor at term. Twelve cases, or 2.5 per cent, followed ectopic gestation. In 6, the character of the previous pregnancy was doubtful. The great majority of their cases, therefore, followed an abnormal pregnancy, yet 21 per cent followed delivery at term, and a pregnancy that had appeared normal.

Hydatidiform mole antedates so many cases that it must be considered as an important predisposing condition. We are ignorant, however, of the percentage of cases of hydatidiform mole that are followed by chorio-epithelioma. In Palmer Findley's first series of 210 hydatidiform moles, 16 per cent were known to become malignant

later. In his series of 500 cases, 31.4 per cent, or 157 cases, were followed by chorio-epithelioma. But Findley calls attention to the fact that ordinary benign moles are not reported, while those which undergo malignant changes are recorded with greater frequency. Senarclans found that of 49 hydatidiform moles, chorioma developed subsequently in 3, or 6 per cent, while 4 others died of other complications. Hitschmann and Cristofolletti, in 200 cases of hydatidiform mole, found that 7.5 per cent were followed by chorio-epithelioma.

Our conception of the frequency of hydatidiform degeneration of the chorion has been materially changed by the work of Arthur Meyer, who found, on gross examination, 8 such cases in the first 2,089 uterine abortions in the Mall collection, or one in 261; careful microscopic examination showed a much higher proportion. These findings justify his conclusion that hydatid degeneration is not uncommon in early abortions. Later, it appears more rarely as former statistics would indicate. Madame Boivin, in 1827, found 1 mole in 20,000 pregnancies; Williamson, in 1900, 1 in 2,400; Pozzi met with none in 6,000 cases; Mayer, in 1911, in 3,105 pregnancies, found 10 cases; Essen-Müller, in 6,000 cases, found a proportion of 1 to 333 cases. We have met but 1 case in the last 3,600 pregnancies. Yet, in view of Arthur Meyer's findings, fewer moles are the forerunners of chorio-epithelioma than has generally been considered, since the type which he studied showed a decided tendency to abort completely at a very early period in pregnancy.

Age.—The age of cases presenting chorio-epithelioma ranges from seventeen to fifty-eight years in cases reported in the literature. Teacher, in 188 collected cases, found thirty-three years as the average age. Fifty-seven per cent of his series occurred between twenty and forty years. There were 6 cases under twenty years and 9 cases over fifty years. In Vineberg's collection of 78 cases, 4 were less than twenty and 8 were over fifty years. A number of cases which occurred younger than twenty years and older than fifty years were thought to have followed hydatidiform mole, which is often met with at the extremes of fertile life.

Location of Growth.—In nearly all cases, the tumor has been found located in the uterine cavity. There are, however, undoubted cases of primary ectopic chorio-epithelioma. The latter group have been found chiefly in the tubes and vagina. There is some question as to whether it may arise in the ovary, as an extraplacental tumor.

Tubal pregnancy has given rise to chorio-epithelioma in 21 reported cases. Twelve of these were reported by Risel in 1905 and to this list has been added 1 case by Garkisch, 7 by Liepmann in 1914, and 1 by Hartz in 1916. All of these cases were discovered either at operation or at autopsy. The diagnosis is based upon the presence of a tumor distending the tube or broad ligament and lying wholly outside the

uterus and with a uterine mucosa which is unaffected. The mass has varied in size from that of a hen's egg to that of an adult head. The tumor is very friable and exceedingly hemorrhagic and presents a gross appearance identical with that of tumors which are primary in the uterine cavity. The histologic features are also identical with the growths primary in the uterus. Metastases are very frequent. The tumor seems to have a more rapid course and to metastasize more quickly than does chorio-epithelioma of the uterus. Albert's case and that of Hartz are the only ones which recovered.

There are a number of tumors which have been described both in the testicle and in the ovary which have presented structures identical with those of chorio-epithelioma without evidence of teratomatous features. They are now usually considered as teratoma, although for a time they threatened to overthrow our ideas concerning the significance and mode of origin of chorio-epithelioma. They were first explained on the ground that fetal membranes had been included in the teratoma which proliferated only after lying dormant for many years. Nearly all investigators now accept the view of Risel that such an assumption is unnecessary, since such a tumor may develop from undifferentiated fetal ectoderm present in the teratomatous growth.

Waldeyer, in 1868, described a polypoid tumor mass suggesting a hydatidiform mole which extended from a testicular teratoma into the pelvic veins. Breus, in 1878, described a similar case in which the polypoid masses extended into the heart. There are, in the French literature, a number of similar cases described under the term "sarcoma angioplastique" recorded by Malassez and Monod, Carnot and Marie, and others who also noted the resemblance to hydatidiform mole. McCallum observed a similar case which he interpreted as lymphendothelioma. Wlassow and Schlagenhauser, however, were the first to emphasize the resemblance of this type of tumor to the chorio-epithelioma. Their report made a profound sensation and has been the cause of much investigation. Their case presented a teratoma of the testicle which had given off generalized metastases and was composed of syncytium, Langhans' cells and occasional structures suggesting chorionic villi. They traced the origin of the syncytial masses to the epithelium of the testicular growth, identified the Langhans' cells and described glycogen in them, noted the hemorrhagic character of the metastases, and showed that this chorioma of the testicle reproduced almost exactly the essential features of chorio-epithelioma of the uterus.

Similar processes have been noted in the ovary where, of course, there is the possibility that the tumor followed an ovarian pregnancy. The reported cases are few in comparison with those of chorioma testis. Pick early described a case which reproduced the gross features and

microscopic picture of a primary chorio-epithelioma of the uterus. The mass was composed of syncytial and Langhans' cells derivatives, together with a sarcomatous framework. The syncytial masses were traced to a neuro-epithelial cell group, invaded the vessels and added a hemorrhagic character to the tumor. The growth contained many small polyhedral cells of the Langhans' type which presented many mitoses and contained glycogen. The mass also presented glandular areas lined with mucous cells in a sarcomatous framework. Emil Ries, in 1915, reported 1 case and collected 6 others from the literature, all of which presented as primary chorioma of the ovary without evidence of other teratomatous structures. Ries carefully reviewed the various possibilities concerning the origin of his tumor: (1) it might have been of teratomatous origin; (2) a metastases from a chorioma primary in the placenta which was expelled completely during labor; (3) it might have developed from fetal cells which were deported from a normal placenta and which did not assume malignant character until it reached the ovary; and (4) it might have arisen from an ovarian pregnancy.

There are also a number of cases which have been described as primary ectopic chorio-epithelioma in locations remote from the various possible placental sites, and in which it was impossible to trace a direct anatomic connection between the growth and any site of an intra-uterine or extra-uterine pregnancy. Palmer Findley, in 1904, collected 21 such cases and since then many others have been added. The uterine mucosa is always free from involvement, although it may contain typical decidual alteration. The endometrium in the cases of Schmorl, Fiedler, and Holzapfel averaged .8 centimeter in thickness and resembled a decidua vera of normal pregnancy. It seemed analogous to the decidual formation of ectopic pregnancy. The entire group is composed of cases where the lesion could be directly inspected, that is, in the vagina, labium and cervix. The clinical diagnosis was at all times confirmed by microscopic examinations of tissue curetted from the uterus. While much has been written concerning these primary ectopic chorio-epithelioma, nearly all agree that they are but metastases which developed a considerable time after the primary growth, which was situated in a placenta, or in a hydatidiform mole, which had been expelled from the uterus. There is also the possibility alluded to before that these so-called primary ectopic chorioma develop from embolic cells in a normal placenta which assume malignant properties only after they have been arrested after being deported. Not all, however, accept these possibilities, since there is a chance that some of the growths considered as primary ectopic choriomata of the tubes, ovaries, and other organs were not derived from either teratomatous sources or products of gestation. Risel, when reviewing the subject, stated that many of the tumors on record might well be metastases

from carcinoma or sarcoma whose secondary metastases developed an atypical structure. Others, however, believe that Risel's restrictions were too rigid and claimed that the heterotopic chorio-epithelioma in both sexes present identical histology with chorio-epithelioma which are primary in the uterus, whereas, the choriomalike structures developing in metastases from carcinoma or sarcoma present varying appearances and only a few resemble chorio-epithelioma. All agree that a proper diagnosis cannot be made from fragments of tissues since microscopic resemblances may be very misleading.

Period of Latency Following Pregnancy.—The period of latency, or the period elapsing between the last pregnancy and the development of the disease, is most variable, and has ranged from a few weeks to several years. The longest interval stated is thirty-one years (Paltauf and Polosson). The interval is often from three to four years; in Caturani's case it was five years, and in Polano's case, ten years. Many investigators doubt the accuracy of the long period of latency and assume that an early abortion has been overlooked. Yet there are a number of cases which must be accepted where the interval was at least five years. One of these was reported by Kroesing. The patient was fifty-two years of age. Five and a half years before, a hydatidiform mole had been removed. Two and a half years later, both ovaries were removed. At this time, the uterus was perfectly normal. Following the operation, there was complete amenorrhea. Three and a quarter years later, or five and a half years after the hydatid, the uterus was removed for metrorrhagia and was found to be the seat of chorio-epithelioma.

The observation of Emil Ries suggests that a villus may preserve its identity in the uterus for many years. In studying a uterus which he had removed for fibroids from a woman who had not been pregnant for eighteen years, he noticed a long threadlike formation several inches long in the uterine cavity, attached to blood sinuses in the left uterine horn. Microscopic examination showed that these filaments had histologic structures identical with those of chorionic villi, except that the investigator was not able to convince himself that the cellular covering was syncytium. The masses did not arise from the muscular coat of the blood vessels but penetrated them. They were not, in consequence, "vein myoma." The longer filaments presented the outline of primary chorionic stalks of early pregnancy, save that they were two or three times as long. Others, who casually studied his sections, thought that they could discern a double layer of fetal ectoderm. While there may be some doubt concerning the nature of the epithelial covering, that is, whether it was covered with altered endothelium of the veins, there is no question but that there was no proliferation of the cells. Lack of this phenomena may explain the failure of the mass to develop into a typical chorio-epithelioma.

There is no doubt but that, in many cases, with a latent period of a few weeks, that the growth was present before the pregnancy was ended. Vineberg found a chorio-epithelioma in the uterus when exploring the cavity of that organ with his finger, immediately after removing a hydatidiform mole. Similar cases have been reported by Eden, Kelly, and Workman. In Pick's case, a chorio-epithelioma was observed to develop in the vagina during the fourth month of gestation, while the uterus still contained a hydatidiform mole. Wallart found a metastatic growth in the eighth month of pregnancy and metastatic nodules in the vagina have been observed while the uterus still contained a hydatidiform mole (von Rosthorn, Poten, and Vassmer). Branson observed, during labor at the eighth month, what appeared to be a chorio-epithelioma. The mass was attached to the external os and part of it broke away when he introduced the forceps. The patient had complained of symptoms suggestive of cerebral metastases for some time before delivery. She died a few days after labor. There was no autopsy. Fink's case presented symptoms so shortly after labor at the thirty-sixth week that he thinks that the tumor was present before delivery. There are similar cases in the literature which substantiated his belief. Fink's patient had a severe post-partum hemorrhage following a spontaneous separation of placenta. There was more than normal lochia during the puerperium. The uterus appeared subinvolved. Bleeding recurred on the eighteenth day and two days later, he removed a polypoid growth with the curette which was found to be suspicious of chorio-epithelioma. Bovee found an early chorioma in a two-month chorion in a uterus which he removed for degenerating fibromyoma.

Metastases.—Metastases in chorio-epithelioma occur in nearly all cases. They appear at a varying period and sometimes occur at a very early stage. Thus, Poten and Vassmer excised 2 vaginal tumors (metastases) five days before the primary tumor was detected in the uterus. Metastases usually takes place through the blood current, which is explained by the tendency of fetal ectodermal cells to erode and penetrate the blood vessels with which they come in contact. General metastases result from fragments of the neoplasm which invade the blood vessels and are carried to the heart, and thence to the lungs from which it is disseminated to all the organs. Metastases to the organs of the genital tract develop from cell structures which pass through the venous anastomosis of the pelvic organs. Nearly all organs of the body have been the seat of metastases.

Metastases in the lungs are most frequent. They vary much in number and size. Occasionally, only one tumor is found which may acquire very large dimensions; more frequently, numerous small nodules are scattered throughout the entire lung. The apices and bases are commonly involved and the middle lobes less frequently.

The secondary growths may develop insidiously and give no evidence of their presence until found at autopsy. More frequently, they cause hemoptysis, dyspnea and pain in the chest. Quite naturally, the symptoms are dependent upon the site, number and size of the secondary growths. The cases of Lindfors and Morison presented metastases of enormous size. Quite often, the lung is fairly riddled with the growths.

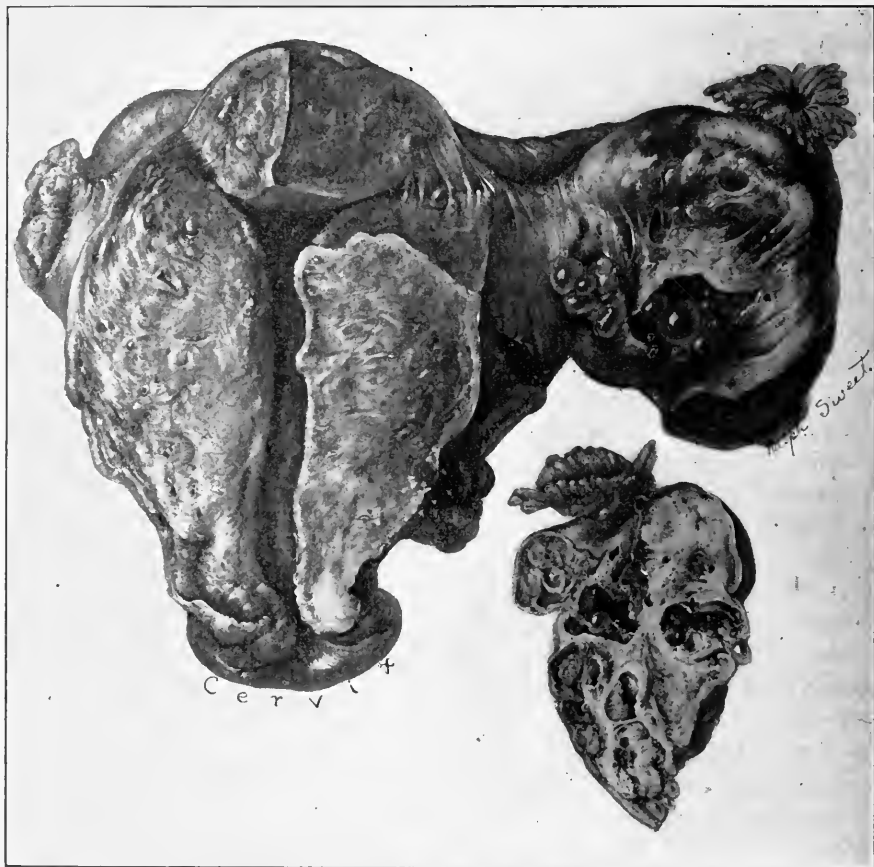


FIG. 68.—CHORIOEPITHELIOMA. A chorio-adenoma developing shortly after the removal of a hydatidiform mole. The growth has invaded the uterus and does not present as a polyp. The extension into the broad ligament is most marked on the right side where vesicular masses may be seen invading even the tube and ovary. (Case and illustration through courtesy of Dr. Harold Brunn.)

Next to the lungs, the vagina and vulva are most commonly involved. Because of their situation, they are the most easily discerned. Occasionally, a single isolated tumor only is present. More frequently, there are numerous small nodules which may almost coalesce and nearly form a ring. Their form and size vary almost as much as their location. They may involve the entire vaginal canal

or they may occur only at the vulvar orifice or in the folds of the labia majora. They often occur as small nodular masses beneath the mucosa, characterized by brown or violet discoloration. They have been likened to thrombosed varices which they resemble so closely as to be mistaken frequently for them. The consistency is tense and elastic, almost fluctuating at times. Metastases in these areas grow very rapidly, cause necrosis and irregular ulcerations. The latter are usually clean cut and well defined, but soon cause profuse and obstinate hemorrhage and become infected. They then give rise to a sanguineous, fetid discharge. The time at which metastases appear varies considerably. Usually they occur late in the disease, often when there is advanced cachexia but occasionally they occur so early that they may constitute the first sign of the disease.

Secondary growths in the liver are frequently found at autopsy. Usually they are widely disseminated and rather small in size, ranging from 1 centimeter to 3 or 4 centimeters. Hitschmann's case presented a liver which was literally riddled with the metastatic nodules. Paviot observed a case in which there was a tumor 4 centimeters in diameter on the convex surface and many other growths in the depths of the organ. Liver metastases do not usually give rise to symptoms. Krawer and Macaggi described an increased size of the liver in their case, yet this condition is not always noted. A secondary tumor the size of a fetal head was not even suspected in the case of Schmorl.

Kidney metastases have been described by Nitzel, Tibaldi, Gottschalk, and many others. These growths are usually small and give no symptoms. Thus, the well-observed case of Davis and Harris gave no symptoms, although a tumor in the left kidney was 6 centimeters in diameter. The urine in Gottschalk's case contained characteristic plasmoidal masses. The tumor, however, was the size of a fetal head. Secondary growths have rarely been observed in the ureter (J. Schmidt), in the bladder (Jacubasch, Krawer, Perski, Marchand), and in the urethral wall (Holzapfel).

Metastases in the central nervous system are also common. They occur most often in the occipital lobes on the left side. They may be multiple, yet are often single and vary in size from a minute growth to that of a hen's egg. Metastases in the brain do not usually have the hemorrhagic appearance of the visceral metastases. Secondary growths are occasionally noted in the cord. Kedrierski and others have reported cases.

In addition to these sites, metastases have been found in the most diverse organs, as for instance, in the stomach, large and small intestines, heart, pericardium, pancreas, spleen, thyroid, suprarenal capsules, diaphragm, bone and subcutaneous tissue.

Ovarian Changes, Associated with Chorioma.—The ovarian changes in chorio-epithelioma constitute an interesting feature. Wil-

ton, in 1840, described cystic changes in the ovaries in a case of a malignant mole; since then, many others have reported similar findings. In 1895, Marchand called attention to the frequency of ovarian cysts in chorio-epithelioma cases. Patellani, in 1905, found that, of 68 cases reported up to that time, 62, or 91 per cent, presented bilateral cystic changes. Since then, it has been seen that this percentage is probably too high unless one includes marked grades of the small cystic cavities seen in ovaries. There is no doubt, however, but that pronounced cystic changes in both ovaries occur so frequently with chorio-epithelioma as to constitute a specific anatomical feature of the disease. It is of interest that in several cases, the cysts receded in size after the extirpation of the tumor or mole, although they persisted in the cases progressing to death.

The cysts may be very numerous and small or present as multilocular changes the size of an orange. The contents are thin, yellowish, serous fluid containing albumins, lipoids, and a little mucin. The walls of the large cysts are lined by a deep layer of large over-nourished granular polyhedral cells, resembling exactly the lutein cells of the early corpus luteum.

The origin of the cysts has not been definitely determined. Jaffe and Orthmann feel that most of them arise by distention and overgrowth of corpora lutea. The small multiple cysts of gestation are not so clearly traced. Seitz thinks that they arise from atresic follicles of the ovary which begin to hypertrophy in the sixth week of pregnancy and continue to term. He believes that these follicles have no relation to the corpora lutea. Stöckel finds that the theca cells of the follicles may wander out into the ovarian stroma during pregnancy and form lutein cell groups from which the small cysts arise. Schaller and Pforinger describe such cell groups in their case which were so abundant as to suggest a tumor process. The majority believe that the cysts represent a disorder of lutein secretion.

L. Fränkel advanced the view that the disturbance of the lutein function induced by the cyst caused the death of the ovum and the production of the tumor since excision of the corpus luteum prevented implantation and development of the ovum. The latter part of this theory does not appear substantiated. L. Pick interpreted a cyst as evidence of hypersecretion leading to proliferation of the chorion. Veit considers the possibility that a primary ovarian disease yields a diseased ovum which degenerates and entails abnormal proliferation in the chorion. Against this theory, there is the fact that chorio-epithelioma may follow a normal labor. The suggestions that the cysts result from venous congestion (Seitz), that they are equally characteristic of normal pregnancy (Wallart), and that they belong to the ordinary nutritional changes of pregnancy (Dungen), also are disproved.

Symptoms.—The symptoms may be divided accordingly as they

arise from the uterine tumor or from the metastases. The latter may be subjective or objective.

The most characteristic and prominent symptom of the primary uterine tumor is hemorrhage. This, as a rule, is very profuse and may even be alarming. In one of Vineberg's cases, the second hemorrhage was so great that it would have caused death had it not been arrested by packing. Yet, in many instances, the bleeding may be comparatively slight, although protracted, simulating that which arises from retention of membranes or placental remnants. In very rare instances, there may be no bleeding, even though the growth is situated at the placental site as in the case of Lichtenstein. Amenorrhea of three or four months duration has been observed in a few cases (Eden, Caturani). This singular phenomenon has been observed only in cases following hydatidiform mole.

Intraperitoneal hemorrhage has been responsible for the initial symptom in cases which, in their growth, perforated the uterus and simulated a ruptured tubal pregnancy. Erck and Outerbridge reported such a case in a woman of twenty-seven who developed these symptoms six months after an incomplete abortion suggestive of hydatidiform mole. They collected 8 similar cases from the literature. Hyde, in 1915, reported 1 other.

There are a number of cases in the literature in which the patients were curetted for bleeding of rather moderate amount but the symptom was not arrested by the treatment. In quite a few instances, the patient was curetted as many as four or five or even six times before the condition was suspected. Suspicion of the presence of a chorio-epithelioma should be aroused when a careful curetting shortly after pregnancy fails to arrest bleeding.

The hemorrhage soon leads to anemia with its train of symptoms. Cachexia develops, the patient feels and looks ill, and the septic condition may intervene. The latter is particularly apt to occur when the case has been curetted several times. Occasionally, there is complaint of uterine cramps caused by the expulsion of blood clots or débris of the growth. Pollosson and Violet called attention to this symptom.

Occasionally, the first manifestations of the disease may be symptoms from metastases. They are most likely to present in cases with involvement of the lung. A. Straume reports such a case which was diagnosed as pulmonary tuberculosis on account of hemoptysis, dyspnea, and pain in the chest. The patient had had no uterine bleeding, nor had she given a history of recent pregnancy. The initial symptoms are rarely due to cerebral or spinal tumor. A. Kedrierski reports a case in which paraplegia was the initial symptom, developing 8 months after a pregnancy at term. The autopsy disclosed a chorioma in the spinal cord at the level of the fourth lumbar vertebra. Other metastases were found in the lungs and liver. There was no uterine

tumor. Although metastases in the kidney have frequently been described, symptoms resulted only in the case of Gottschalk in which the urine contained characteristic plasmoidal masses. The tumor in this case, however, was the size of a fetal head. The involvement of the broad ligament is frequently attended with pain.

Objective symptoms may be offered by the presence of vaginal or vulval metastases. They appear most frequently in the anterior wall near the urethral meatus. They vary in size from that of an almond to a hen's egg; the larger growths are usually single. They possess a deep bluish color and appear very vascular.

In the rapidly growing, highly malignant forms, symptoms of intoxication soon appear as a result of decomposition of the tumor masses, or from actual infection. A foul vaginal discharge is noted, there is fever of irregular course, and the woman rapidly becomes emaciated. Occasionally, chills and high fever are present, which are due not so much to the septic process as to extensive metastases. While septic conditions of the primary tumor are not uncommon, pyemia does not develop, nor have organisms been found in the metastatic tumors.

Diagnosis.—The diagnosis of chorio-epithelioma is often attended with difficulty. The condition should be suspected when profuse hemorrhage follows a hydatidiform mole that had been thoroughly removed. Vineberg recommends that, when removing a mole, the uterine wall should be thoroughly explored with the finger for any suspicious nodule or any thin area of the wall. The diagnosis may occasionally be made in this manner when the tumor is very early. Vineberg reports two such cases and Eden one. The cervix is usually patulous when the growth follows shortly after labor at full term so that it is possible to palpate the interior of the uterus with the finger. The presence of an elevated, fairly hard nodule with an excavation in the center is almost pathognomonic. The diagnosis is practically absolute when the characteristic reddish blue papules appear on the vagina or in the vulva.

The greatest difficulties are encountered when the growth follows an early miscarriage because in such cases one cannot be certain that the bleeding did not follow the retention of placental remnants even though the case had been treated by curettage. One must then turn to the microscope to complete the diagnosis, although the evidence may not be conclusive and may even be misleading. One naturally hesitates to remove the uterus of a young woman in the absence of definite clinical evidence and in the presence of only suspicious material removed by the curette. Vineberg recommends that both the interior and exterior of the uterus be palpated and inspected in such cases, obtaining exposure by inverting a part of the uterus after a vaginal hysterotomy and colpotomy.

MICROSCOPIC DIAGNOSIS.—The microscopic picture of the tumor in the

uterus is perfectly definite. Yet there is much difficulty in diagnosing many of these tumors only from curettings. The presence of trophoblastic tissue in the uterus without villi three or four weeks after a pregnancy gives a positive diagnosis. When villi are present, the diagnosis is more difficult, yet in such cases one should not forget the possibility that there is a malignant mole. No precise statement can be made as to the amount and character of epithelial overgrowth which will warrant a diagnosis of malignancy. There is normally present for some weeks after a pregnancy a certain amount of infiltration of the endometrium by trophoblastic elements. Such an infiltration is more marked after a hydatidiform mole in which there is also evidence of necrosis of maternal tissues and infiltration of the muscular wall. Robert Meyer defines the position of the microscope in curettings as follows:

"So long as portions of the placenta are present, the recognition of hemorrhagic and necrotic tissues, leukocytic infiltration and cells of Langhans within the mucous membranes is insufficient to justify the diagnosis of chorio-epithelioma, since these also form a part of the picture of placental retention. The significance of the same discovery in the uterine muscle is much more difficult to estimate. Only when one can be quite certain that all villus remnants have been removed, is it possible to reckon on the disappearance of the chorionic epithelial elements in the muscle in from two to three weeks. After this time, should suspicious materials be expelled, or should a new curettage bring to light fresh masses of chorionic epithelium, then, no matter what the condition, they must be regarded as suspicious. Before this time, the recognition of large epithelial and epitheloid cells of varying form with large or grouped nuclei, and multinucleated giant cells, by no means justify the diagnosis of malignant tumor, even when they appear in long processes and broad masses and replace and break through the walls of vessels, for this chorionic invasion can occur apart from malignant new formation."

While much doubt must attend the study of scrapings shortly after pregnancy, there can be no question of the meaning of the characteristic cells removed by scraping the interior of the uterus several months or years after the pregnancy. They indicate an abnormal condition and should be treated as such.

DIFFERENTIAL DIAGNOSIS.—Cases of chorio-epithelioma must carefully be excluded from examples of septic infection in the presence of retained products of conception. Sloughing fibroids, and, rarely, sarcoma or carcinoma of the uterus, may be confused with late chorio-epithelioma. Usually, slight bleeding, fever, and a purulent vaginal discharge coming on shortly after the interruption of pregnancy and

associated with an enlarged uterus containing masses of broken down tissue form a picture suggestive of puerperal infection. Yet if the pregnancy had been a hydatidiform mole, the case should be regarded with the greatest suspicion. The chorioma, on account of its friability, can be readily and thoroughly removed by a curette, leaving the uterine wall smooth and uniform. This treatment should be reserved for the most suspicious cases for, while the neoplasm is benefited temporarily, the condition of the abortion case may be made worse. The hemorrhage soon recurs and the uterine cavity again becomes filled with large quantities of soft tissues in the chorioma cases. The rapid reformation (in two to four weeks) of the tissue *débris* is characteristic of the disease and, in the opinion of Veit, serves to distinguish it from the septic retained products of conception.

Prognosis.—Taken as a whole, the chorio-epithelioma group are the most malignant tumors known. Death usually takes place within a year. Yet the prognosis is complicated by the fact that certain cases have recovered spontaneously or after simple curettage or other incomplete operations, even in the presence of metastases. Nor is it possible to classify such cases according to their histologic picture.

In 1904, von Velits collected 8 cases of chorioma in which curettage was followed by recovery. Ewing states that 5 of them were composed chiefly of large wandering syncytial cells which were not accompanied by proliferating masses of Langhans' cells. He, therefore, classified the 5 cases as syncytioma or syncytial endometritis for which Menge recommended curettage as the operation of choice. Of the remaining cases, according to Ewing's analysis, Risel's and Blumreich's were hydatidiform moles, with active proliferation of cells, probably chorionadenoma. Graefe's case was inadequately described. Yet Geist, in 1921, reported a case of typical choriocarcinoma which made a perfect recovery following curettage without any subsequent treatment.

In a number of cases, Marchand, Noble, Kolomenkin, Fleischmann, Hörmann, Dungen, and Cazin-Segoud, the patient recovered after operation, although the tumor was incompletely removed. In all of these instances, the proliferating Langhans' cells were missing and the tumors consisted chiefly of syncytial masses. In Dungen's case, there was recovery after an early hysterectomy for chorioma, and shortly after a vaginal tumor developed but spontaneously disappeared. This case is similar to Schlagenhauser's and suggests the possibility that isolated metastases of choriocarcinoma may spontaneously disappear. In Noble's case, the size of the tumor, 8 centimeters by 8 centimeters by 7.5 centimeters, indicated that it did not belong to the more malignant group of chorioma, a suspicion which was confirmed by the fact that Langhans' cells were absent from the tumor. Hitschmann and Cristofolletti record a growth, the operation for which was abandoned because of the extent of the tumor, which involved the vagina and

bladder and which had infiltrated through the pelvis. The patient improved rapidly in spite of an incomplete operation. One month later, there were no signs of the tumor of the uterus and the pelvic structures seemed to be free. The patient was in perfect health seven years later.

It is apparent that neither pulmonary nor vaginal metastases carry a necessarily fatal prognosis, although it should be emphasized that the very great majority of cases with cough and hemoptysis speedily succumb. The gravity of vaginal metastases is considerably less serious, since quite harmless growths may result there from deported cells and villi. Yet these cases must merely be regarded as exceptions to the rule that chorio-epithelioma are extremely malignant tumors.

Von Fleischmann, in 1905, collected the cases of Chrobak, von Franqué, Zagerjanski-Kissel, Ladinski, Neumann, Schauta, and Pestalozzi, all of which recovered after probable occurrence of metastases in the lungs. The evidence of pulmonary metastases consisted of cough and hemoptysis, and there was no reasonable doubt but that cell emboli occurred and were eventually absorbed. This conclusion has been rendered more acceptable by what has been learned more recently concerning the nature of pulmonary emboli from the normal placenta and their usual fate. It is possible that some of the emboli consisted only of fibrin, yet Risel, Eden, and Lockyer, have noted healed nodules in the lungs surrounded by others which were still growing in cases which terminated fatally. Teacher has made a similar observation.

There are a larger number of cases in which recovery has resulted after the development of vaginal metastases, and it is in these that there is a conflict of opinion as to the value of histologic examinations of excised tissue. Schmauch collected 13 cases which recovered in spite of the fact that vaginal metastases developed. Neumann and Kolomenkin reported 2 others. The observation of Rockafellow is most remarkable. In some of the cases, the uterus and vaginal nodules were removed at operation. In others, only the uterus was removed, while in the cases of Fleischmann, Hörrmann and Kolomenkin, neither the uterus nor vaginal nodules were completely removed. In Rockafellow's case, the uterus was removed but large growths recurred in the labia every few weeks. Sometimes, they were as large as a kidney, and, when excised, they returned in a week or so. After four operations for recurrences, the patient's condition became so poor that it did not seem worth while to again attempt removal. To every one's surprise, the growths began to shrink spontaneously and disappeared in a few weeks, leaving only a hard ridge to indicate their former site. The patient began to improve and in a short time regained good health and remained so while she was under observation, which was more than two years.

Ewing contends that a study of the case reports clearly indicates that the cases which recovered after pulmonary and vaginal metastases belong to his group of chorio-adenoma, or syncytioma, and not to the choriocarcinoma, and that histologic examination is of much value as a guide to prognosis. In 15 cases, villi were present in 9, in 3 the growth was atypical, while in 2 the description was indefinite. He admits that Schlagenhauser's case was possibly choriocarcinoma, although the syncytial cells were very abundant and extremely vacuolated as in chorio-adenoma. The nodule was small, and the uterus was normal. Yet this review has received no confirmation from the works of others. Vineberg does not accept it, nor is it confirmed by the work of Geist; moreover, it appears that in Schmauch's compilation, there were many deaths in cases in which syncytial cells were the predominating feature in the lungs and vagina, and that Langhans' cell masses were deficient or absent. There were also several chorio-adenoma in this group. Yet, according to Ewing, one must be impressed by the fact that death in these cases has often resulted from more or less accidental conditions, such as hemorrhage and infection, rather than from the progressive growth of the tumor.

Geist, whose study is quoted, believes, moreover, that Ewing is too pessimistic in his prognosis for the cases presenting as choriocarcinoma. Geist's series included 14 cases, 10 of which were choriocarcinoma, of which only 3 died. Moreover, 1 case presenting curettings typical of choriocarcinoma recovered following curetting without other operative procedures.

In the light of the gloomy prognosis given usually to chorio-epithelioma, it is refreshing also to turn to Vineberg's most remarkable series. He records 9 cases, only 1 of which died, a patient developing sepsis following curettage and packing. Unfortunately, he does not state the exact microscopic pathology. He does say, however, that his "unusually excellent results cannot well be explained by the mere assumption that all his cases were of a semibenign variety as that would be a fortuitous occurrence, not paralleled by a series of a similar number of cases in the literature." He feels that it is more within reason to attribute the results to the fact that the diagnosis was made at an early stage of the disease than to the assumption that every growth was of a nonmalignant type.

Teacher has arranged his collected series of 188 cases to show the relation of the mortality to the type of pregnancy which antedated the tumor. There were 73 cases which followed a hydatidiform mole with a mortality of 53.4 per cent. There were 59 cases which followed an abortion with a mortality of 66.1 per cent. Following labor at term, there were 49 cases, with a mortality of 79.6 per cent. Seven ectopic choriomata were included in his study, only 1 of which recovered. Radical operation was performed only 99 times with 36.4 per cent mor-

tality. Recurrences were noted within six months, or not at all, except in 5 cases. In 1 case (Löblein), recurrences did not develop for one year. The high mortality in the cases following labor at term is very striking.

Treatment.—There is not a uniform agreement as to the proper method of treatment as one would expect at first sight, of a tumor which arises from the uterus and which is usually classed as the most malignant of all neoplasms. Aside from the fact that there may be considerable difficulty in determining the diagnosis, the essentials of treatment may be confused because the uterus may not contain a tumor (the disease presenting as metastases) and because many cases have been cured by curetting alone. Although there are many who argue for minor measures, there is no doubt but that the routine performance of a hysterectomy, together with the removal of local growths will appeal to nearly any surgeon as a rational procedure. Some, as Ewing, believe that conservative treatment is indicated in the presence of less advanced growths and especially in young women, arguing that the first treatment should consist only in a curettage and the removal of vaginal metastases. If the symptoms recur, hysterectomy is then indicated. Justification for such a plan of treatment cannot be obtained from the history of other neoplasms. It has resulted because in the earlier cases, the tumor was thought to metastasize so early that the removal of the uterus alone would not improve the situation. Active treatment, in consequence, was not undertaken after the diagnosis had been made from curettings. Yet the study of many such cases who, although abandoned to their fate, presently came to recovery, showed that the tumor was not invariably fatal and that recovery might follow from distinctly minor measures. A policy of delay, in the light of Vineberg's remarkable results, no longer seems indicated.

Schmauch and Ewing are in accord with the statement that operation is contra-indicated and merely hastens the fatal issue when metastases have occurred. On the contrary, there are cases in the literature which have recovered after incomplete operation even when the findings indicated that the tumor was really choriocarcinoma. Geist, especially, states that a diagnosis of choriocarcinoma, even with metastases, is not necessarily fatal. There is so much chance of error in a diagnosis from scrapings or from structures removed from vaginal metastases that any surgeon should feel the responsibility of refusing hysterectomy.

Repeated curetting seems to be an extremely dangerous procedure, since it is prone to set free particles of growth which may escape into the circulation and cause metastases. Hitschmann and Cristofoletti studied 300 cases in the German literature and made a comparison between the results of cases that were curetted and those that were not curetted. The metastases were much more extensive and rapid in the former group. They also found that the cases who had died without operation had, as a rule, fewer metastases than those who

were subjected to hysterectomy. Especially did the trauma incidental to vaginal hysterectomy cause widespread metastases.

The abdominal panhysterectomy is the method of choice, because of the fact that it necessitates less trauma than the vaginal operation. Hitschmann and Cristofolletti advise the excision of the deep pelvic veins which are frequently filled with extensions from the growth. Vineberg does not agree, stating that the venous extensions frequently disappear spontaneously. We advise the most extensive removal that the individual case will stand.

Radium.—Radium has not been tried in enough cases to warrant conclusions as to its value. There is no doubt that there may be trauma attending its insertion. Ewing calls attention to the danger of hemorrhage following its application. In Erck and Outerbridge's case, it was employed for the treatment of an extensive recurrence which was causing alarming hemorrhage six weeks after a supravaginal hysterectomy. At time of operation, the case presented an extensive chorio-epithelioma which had penetrated the uterine wall and given rise to a severe intra-abdominal hemorrhage. A month after the radium treatment, the patient was subjectively well. There is no later report of the case. Clark, in 1921, reports 2 cases treated for hemorrhage which are still alive between six and seven years. There are also a few cases noted in the German literature. We have tried it in one case unsuccessfully. The case was a typical chorio-epithelioma and received 3,420 mc. hours without producing marked change.

While an insufficient number of cases have been reported to enable one to speak from actual results, radium from the theoretical standpoint appears as the logical treatment of this condition.

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CHAPTER XII

TUMORS OF THE OVARY

Classification—Frequency—Nonproliferating cysts—Follicle cysts—Corpus luteum cysts—Blood cysts of the ovary—Retention cysts not derived from the follicle—Tubo-ovarian cysts—Symptoms—Diagnosis—Treatment—Parenchymatogenous tumors—Epithelial tumors—Histogenesis—Pseudomucinous cystadenoma—Microscopic picture—Solid adenoma—Serous cystadenoma—Racemose ovarian cysts—Myxomatous degeneration of surface papillae—Other adenoma—Ovarian carcinoma—Etiology—Age—Classification—Solid ovarian carcinoma—Cystic carcinoma—Adenocarcinoma pseudomucinum—Primary squamous-cell epithelioma—Atypical forms—Clear-cell cancer—Carcinoma resembling lymphosarcoma—Krukenberg tumors—Metastatic carcinoma—Clinical features of ovarian cancer—Stages of growth—Lymph gland involvement—Involvement of neighboring organs—Symptoms—Complications—Diagnosis—Treatment—Prognosis—Embryoma—Etiology—Cystic dermoids—Frequency—Age—Appearance and form—Structure—Atypical forms of dermoids—Multiple dermoids—Malignant degeneration dermoids—Symptoms—Diagnosis—Treatment—Prognosis—Teratoma—Struma ovarii—Symptoms—Diagnosis—Treatment—Prognosis—Stromatogenous tumors—Fibroma and myoma—Symptoms—Diagnosis—Prognosis—Treatment—Osteoma and chondroma—Myxoma—Angioma—Sarcoma—Adenomyoma—Mesonephric tumors—Malignant tumors of corpus luteum—General symptoms of ovarian tumors—Complications—Torsion—Causes—Symptoms.

Because the ovary contains such an extraordinary variety of energetic cellular elements, it is more likely to be the seat of tumor formation than any other structure in the body. Under the general heading of ovarian tumors are included not only the true neoplasms, but a group of tumors which are usually regarded as the result of inflammatory changes.

Classification.—A number of classifications have been proposed, although none are completely satisfactory. The oldest divided the growths into cystic and solid tumors and was of service at a time when the operative treatment consisted chiefly in tapping. Later, a division into benign and malignant tumors was attempted. Waldeyer early sought a classification according to the histogenesis, and divided them into epithelial and connective tissue tumors. Pfannenstiel proposed an elaborate classification which at least forms the basis for the majority of recent authors. He presented the subject in three main divisions: (1) nonproliferating cysts; (2) new formations; and (3) mixed tumors. The new formations were divided further into parenchymatogenous and stromatogenous tumors. The details of the classification are as follows:

- I. Nonproliferating cysts
(Follicular cysts; cysts of the corpus luteum)
- II. New formations
 - A. Parenchymatogenous tumors
(Tumors arising from germinal or follicular epithelium, or from the ovum)
 1. Epithelial new formations
 - a. Cystoma serosum simplex
(Simple cyst)
 - b. Cystadenoma

{	Pseudomucinosum (Multilocular cysts)
{	Serosum (Papillary cysts)
 - c. Carcinoma
 2. Embryomata
(Tumors springing from the ovum)
 - a. Dermoid cysts
 - b. Teratomata
 - B. Stromatogenous tumors
(Tumors arising from the connective tissue)
 1. Fibroma
 2. Sarcoma
 3. Perithelioma and Endothelioma
- III. Mixed tumors
(Various combinations of the tumor processes enumerated)

This classification will be followed in the main, with a few unimportant changes.

Frequency.—Ovarian tumors were found in 1.4 per cent of 36,158 cases in Martin's clinic. Stander found the relative frequency of a series of 295 cases as follows:

Tumor	Cases	Per cent
Cystadenoma.....	205	69.5
Carcinoma.....	40	13.6
Embryoma.....	26	8.8
Sarcoma.....	20	6.8
Fibroma.....	4	1.4

NONPROLIFERATING CYSTS

The tumors of this group are thought to be retention cysts resulting because of errors in the development or retrogression of graafian follicles. There are two chief types: (1) follicle cysts, which are supposed to be caused by abnormal secretion of atresic follicles; and (2) corpus luteum cysts, which result from incomplete involution of the corpus luteum. They are not classed as true neoplasms. In addition to these, there are a number of cysts which arise as results of inflammatory changes.

Follicle Cysts.—There are two forms: (1) the small cystic degeneration in which the whole cortex of the ovary is converted into a mass of small cysts; and (2) the simple follicle cysts, or hydrops folliculi.

SMALL CYSTIC DEGENERATION OF THE OVARY.—Under this heading, we will consider the type which occurs independent of inflammatory exudate. It is seen often in women with the pubescent type of uterus, frequently in cases with enlarged retroflexed or retroverted uteri, and extremely often when there are varicose veins of the broad ligament. It is believed to result from some chronic circulatory condition which causes a thickening or fibrosis of the stroma of the ovarian cortex which prevents rupture of the enlarging follicles. It may result from mild ascending infections of the genital tract which do not progress far enough to cause adhesions, but which occasion disturbances of the pelvic circulation. All do not agree that it is essentially an abnormal process. Nagel, and others, have urged that it represents only minor departures from the normal follicle. In proof of this, they state that it is occasionally seen in infants who present no pelvic pathology. At any rate, the meaning of the phenomenon is not clear. The picture seen in a single cyst bears a close resemblance to an atresic follicle. Yet, instead of seeing one or two enlarged follicles as in the latter condition, the whole ovary of the small cystic type presents as a cystic mass between the spaces of which there is an extremely dense stroma.

The disease is usually bilateral. The ovary may be somewhat enlarged, although this is not invariable. The tunica albuginea is dense and thickened, except where the small cysts bulge through. Small growing follicles may be found in the stroma between the cysts, although they are few. The hilum contains obliterated blood vessels in which there are hyaline changes. The cysts usually form projections on the surface which may be seen or felt, but the enlargement may lie entirely within the substance of the ovary. The cysts are usually less than 1 and are rarely more than 2 centimeters in size. They contain clear fluid. They may so press upon each other as to cause various irregular shapes which vary greatly from the normal rounded outline. The partition between two cysts may become so thin that a communication between them is eventually established. The cyst wall is lined with a single layer of low cubic, or somewhat flattened epithelium, which, in some places, may be absent or transformed into granular, fatty, or hyaline areas. The ovum and discus proligerus have disappeared. Degenerated epithelium, fat drops, blood corpuscles, and crystals of cholesterin may occasionally be found in the cyst. The ovarian stroma is usually very dense.

SIMPLE FOLLICLE CYSTS.—This condition is also known as hydrops folliculi. The cysts are usually single, and rarely more than two or three are present. They vary in size from 1 or 2 centimeters to 10 or 12 centimeters. The majority are from 3 to 5 centimeters in diam-

eter. The cysts are smooth and globular, with thin transparent walls, and clear serous contents. Rarely, they contain turbid or brown fluid as a result of degeneration or hemorrhage. They are usually situated at one pole of the ovary, although the larger cysts may occupy nearly the entire organ. The surface of the ovary not presenting as a cyst is usually wrinkled and exhibits a thickened tunica. The ovarian stroma may be little altered. The cyst wall is lined by a layer of flattened epithelium, surmounting a connective tissue which is poor in cells. Isolated areas of degeneration may be seen in the epithelial lining. Follicle cysts occasionally present small papillary outgrowths, extending into the cavity. They appear as wartlike excrescences which are regarded as local hyperplasia of the connective tissue, rather than as an outgrowth of epithelium.

The tumors are essentially benign and are believed to develop from atresic follicles. The secretion develops at first from the lining epithelium, and later the mass grows in size from transudates from the blood vessels of the internal theca layers.

Corpus Luteum Cysts.—These cysts are nearly always single and unilocular, although sometimes two may be present. They grow slowly and seldom are larger than 2 or 3 centimeters in diameter, although they may attain the size of a child's head. Their true condition was first recognized by Rokitsansky. They develop usually from mature follicles which do not expel their contents, but in which hemorrhage takes place and involution does not progress normally. They differ from follicle cysts chiefly in that the cystic development occurs in the more advanced stages of the follicle, and that there is a lining of lutein cells.

The tumor is usually found at the pole of a wrinkled, crenated ovary with a thickened tunica. It presents as a thick-walled dark-colored cyst. Infrequently, it is clear. The cyst wall is composed of two layers. The tumor layer is usually thrown into folds. It is yellow or orange-brown in color, and is composed of lutein cells. The outer layer is connective tissue derived from the tunica fibrosa. The lutein layer varies much in appearance, suggesting that the cyst may have different modes of origin. Usually, it presents the characteristic structure of the corpus luteum and consists of large epithelioid cells in a delicate, vascular connective tissue stroma. Occasionally there are no epithelioid cells and the layer consists only of connective tissue. The epithelial lining varies considerably. As a rule, it is composed of a single layer of low cubic or columnar cells lying directly upon the lutein cells. Sometimes there are several layers arranged like squamous epithelium. They may lie directly upon a hyaline connective tissue.

The cysts may contain clear serous fluid, though it may be turbid and dark from extravasation of blood. Calcification of the lutein

hematoma results in the formation of the so-called "ovarian stone," which consists of a hard, calcareous shell, in the center of which is a shrunken blood clot.

Lockyer has called attention to displaced lutein cells occurring in masses or separate from one another in the ovarian stroma. Small cysts may develop from these which appear practically identical with the corpus luteum cyst. These cell remnants are usually described as the so-called interstitial gland.

Bilateral multilocular lutein cysts often occur with hydatidiform mole and chorio-epithelioma. When they occur with the former condition, they return to normal after the uterus is freed from the mole. Some authors classify this type of lutein cyst separately.

Blood Cysts of the Ovary.—These tumors are merely the result of hemorrhage into follicle or corpus luteum cysts. Therefore, they are not pathological entities. The hemorrhage may come from extravasation by capillary hemorrhage or by a larger outpouring of blood at the time of menstruation. Repeated hemorrhages at consecutive menstruations may cause blood cysts of considerable size. Von Franqué states that there is an unusual fragility of the blood vessels in chronic ovaritis. Usually the blood is gradually absorbed so that the cysts do not long remain of much size. Blood cysts undoubtedly form a considerable proportion of the puzzling cases in which an ovarian cyst has been found to disappear completely in a relatively short space of time.

Retention Cysts not Derived from the Follicle.—All the small multiple cysts of the ovary are not of follicular origin. Rarely one may find small translucent multiple cysts upon the surface of the ovary, tubes and their ligaments lined by flat, ciliated, or goblet cells. They are usually regarded as peritoneal inclusions, yet Walthard believes that they arise from undifferentiated germinal epithelium. Babo and von Franqué suggest that they arise from remnants of the primitive nephros. Pick thinks they may develop into cystadenoma.

Tubo-ovarian Cysts.—The simple ovarian cysts may communicate with the fusiform dilatation of the tube, forming a composite cyst of tube and ovary which resembles a glass retort in form. They result from the union of an ovarian cyst with the lumen of a tube which has become adherent to the cyst wall. Thus, an ovarian cyst or abscess may rupture into an adherent tube while the latter is either normal or distended; or a hydrosalpinx or pyosalpinx, when adherent, may burst into a cyst of the ovary. The communication between the two cysts varies; usually definite and circular, it may appear as a thin valvelike partition. Papillomatous cysts of the ovary may break through into a distended tube as may carcinoma of the ovary.

Tubo-ovarian cysts may be unilateral, or bilateral. Their size varies from a few centimeters to 7 or 8 centimeters in diameter. They are

usually unilocular. They are lined in the ovarian compartment by flat cells, and in the tubal section, by cylindrical epithelium. When corpus luteum cysts fuse with the tube, they may be recognized by the presence of lutein cells in the ovarian compartment. The ovarian wall of the cyst is thin and fibrous, while the tubal wall contains smooth muscle. The cyst fluid is usually clear but may be mucoserous, turbid, orange or dark colored.

Symptoms of Nonproliferating Cysts.—The symptoms may vary slightly with tumors of the different groups, yet pain or discomfort constitute the chief complaints. There may be sharp pains a week or two before the period, at the time when the follicle should rupture. Dysmenorrhea is common. The pain may radiate down the thighs, or into the back. Overexertion is often followed by pains. Occasionally there may be only pelvic discomfort often accompanied by various reflex manifestations, such as occipital headaches, nervousness, digestive upsets, and irritability. Menorrhagia is common. Metrorrhagia and scanty menstruation may result from marked destruction of ovarian tissue. A large proportion of women with small cystic ovarian degeneration are sterile.

Pain results when there is extravasation of blood into the cyst or ovarian structure. It is referred to the ovary and may be followed by symptoms of the acute abdomen. It invariably attends torsion of the pedicle, although the severity of the pain varies, depending on the amount of torsion and the suddenness with which it occurs. It often occasions symptoms which when on the right side, are likely to be mistaken for appendicitis.

The reflex symptoms are probably caused by altered ovarian secretion. They may result from increased tension within the cyst.

Diagnosis.—The diagnosis is settled by presence of the tumor. Often it cannot be made with certainty, since the most careful examination may fail to reveal a cyst of small size which has arisen into the abdomen if the patient has firm abdominal muscles and cannot relax well. As a rule, the cystic tumor may be felt by rectal abdominal examination, confirmed by the vaginalabdominal bimanual. The tumor is cystic, and pressure upon it usually causes pain. It does not move immediately when the uterus is pushed about. It is not firmly adherent to the uterus, nor can another ovary be felt upon the same side. Irregularities caused by enlarged follicles may often be felt through the rectum. The sclerotic ovaries give a characteristic feel. The importance of rectal examinations cannot be overemphasized. Occasionally it is difficult to make a diagnosis even under an anesthetic as the cyst may not be under great tension. Broad ligament cysts, or fibroids, unruptured ectopic pregnancies, a thickened tube buried in adhesions, and a chronic appendix must be excluded in the differential diagnosis.

Treatment.—Definite cysts should be treated surgically. The indications for operation in cases of small cystic degeneration are less clear. It is not wise to resort to surgery unless general and local measures are exhausted.

The general treatment consists chiefly in hygiene. The appetite should be stimulated and especial attention paid to the bowels. The patient should be encouraged to avoid heavy work of any kind or anything which will induce fatigue. She should be urged to live as much as possible in the open air and choose a diet of simple and coarse foods. Ovarian extracts usually aggravate the condition and cause hemorrhage.

Locally, counter-irritation occasionally helps a good deal. Painting the vaginal vault with half tincture of iodine every other day for two weeks between the periods may give relief. Pain is often relieved by vaginal tampons, soaked in a solution of ichthyol and glycerin in the proportion of one to ten or one to fifteen, inserted every third day. Hot vaginal douches of soda or weak lysol solutions should be given on the other days. The above outline assumes that the pelvis otherwise presents normally.

Surgical intervention may be warranted in small cystic ovarian degeneration which has been treated faithfully by long-continued general and local treatment without relief, provided only that the surgeon is well acquainted with the necessary refinements of pelvic surgery, since a large proportion of cases are made worse by ordinary surgical treatment. A surgeon can see few more distressing conditions than those caused by abdominal and pelvic adhesions.

Various operative measures have been proposed for the treatment of retention cysts. The following have been described.

PUNCTURE OF RETENTION CYSTS.—Cysts are frequently punctured with a needle, knife or cautery point. It does not seem a reasonable procedure because the cyst lining can rarely be destroyed and there is every evidence that the opening will be closed by adhesions and that the cyst will soon refill. Some have advised burning out the cyst with the actual cautery point. Theoretically, this should be followed by fibrosis, although it is a question how the ovarian tissue takes care of the burn. We do not recommend either operation.

RESECTION OF THE OVARY.—While theoretically ideal, this operation is not followed by good results in the great majority of cases. We have had occasion to reoperate a large number of cases that had been treated in this manner by others. We have never seen a case in which the stump was not covered by firm, dense adhesions. While no one who is not present at an operation can pass judgment on the surgical result, since he is not aware of the primary condition, it seems reasonable to believe that many adhesions occur because of trauma during the operation, and from the subsequent irritation both of the delicate ovarian tissue and

the peritoneum of the intestines by the rough knots of catgut used for the sutures.

If, when the abdomen is opened, the surgeon is convinced that a resection of the ovary promises the best results, it should be done in the following manner: The ovary is held by the gloved hand of the assistant while the operator removes a wedge-shaped piece containing the diseased portions with a very sharp knife. Closure is effected with a No. 00 plain catgut suture, threaded on the finest curved needle that it is possible to use. Raw surfaces should be turned in and the cover made so that only one knot is exposed at the end of the operation. The procedure is technically difficult, because ovarian tissue is friable and does not hold a suture exerting much tension. Moreover, it is often impossible with the naked eye to determine accurately the line of demarcation between healthy and diseased ovarian tissues. Occasionally, a surgeon resects a tumor which is cancerous. We have seen a number of such cases subsequently. The need of immediate laboratory examination of all resected tissues is apparent.

Personally, we do not recommend the operation and rarely employ it, feeling that the majority of cases are made worse as a result of the procedure. In our judgment, it is justifiable only in young women, whose other ovary has been removed, and who are anxious for children.

REMOVAL OF THE OVARY.—It is not often possible to remove the ovary alone without leaving raw surfaces which may invite adhesions. When the ovarian ligament is long, the tumor may be cut away so that the stump of the ligament may be turned under in a smooth manner, yet this is not possible without often causing kinks in the tube. The great majority of cases will be treated far more safely by removing the adnexa of the affected side.

REMOVAL OF OVARY AND TUBE.—This is the logical treatment for growths demanding surgical intervention, since it removes the affected tissue and permits a smooth cover of the raw surfaces. The infundibulopelvic ligament is ligated with No. 2 plain catgut, tied firmly with three knots. The mesosalpinx and meso-ovarium are compressed with clamps and the tube and ovary are cut away. The tube is removed from the uterine cornua by a wedge-shaped incision. The wound thus created is closed with plain catgut in running suture as far as the vessels in the angle of the uterus and broad ligament. These are separately tied. The round ligament is now used to effect a cover. It is tied to the middle portion of the posterior lateral surface of the uterus with linen or silk sutures, after which the stumps of the ovarian vessels, raw surfaces of the broad ligaments, and free edges of the round ligament are turned in with a continuous No. 00 plain catgut suture. If the round ligament is fastened without tension, the normal position of the uterus will not be disturbed. In case the uterus sags, or is posteriorly displaced, or there are varicosities of the pelvic veins, this Webster cover should be supplemented by a suspension on the opposite side.

NEW FORMATIONS

New growths of the ovary may arise either from epithelial or connective tissue elements, that is, parenchymatogenous and stromatogenous tumors. The former are far more common. The tumors may be solid or cystic, benign or malignant.

PARENCHYMATOGENOUS TUMORS

Epithelial Tumors.—These growths may be divided into two main groups, according to the character and methods of growth of the cells: (1) benign tumors, or cystadenomata; and (2) malignant tumors, or carcinomata.

Cystadenomata.—Cystadenomata of the ovary comprise the group of benign tumors which exhibit a glandular, or adenomatous character. They are said to form between 70 per cent and 80 per cent of all ovarian tumors. All cystadenomata are essentially multilocular and are composed of many cystic chambers which result from proliferation of the epithelial cells that line the original cyst. These hypertrophy to form daughter cysts which in turn reproduce themselves, or else form papillary masses which grow into the cyst cavities. Often some cysts grow at the expense of others, which they compress into the lateral wall or else they break through into neighboring cysts, and give the appearance of a unilocular cyst. Careful examination, however, reveals the true character.

Cystadenomata may be variously divided. Abel grouped them into simple cystadenomata or papillary cystadenomata, according as they formed simple cysts, or those with intracystic and superficial papillary processes. Gebhard recognized the similarity between the morphology of ovarian adenomata and uterine carcinomata, and divided them into cystadenomata evertens and invertens. Pfannenstiel, finding a marked difference in the character of the cell secretion, effected a classification upon that basis. He divided them into pseudomucinous and serous cysts. In the former group are included nearly all the simple cystadenomata while the latter group corresponds, with few exceptions, to the papillary cyst. There are exceptions, however, since there may be papillary pseudomucinous cystadenomata and serous cystadenomata without papillary processes.

HISTOGENESIS.—The histogenesis of all the epithelial new formations of the ovary has been much disputed. Indeed, as Goodall states, the more one delves into the subject, the more one is confused by the multiplicity of views and the number of structures from which ovarian tumors may arise. All the various epithelial structures which occur

in or near the ovaries have been accredited with their origin. Thus, the tumors have been said to arise from remnants of müllerian and wolffian tissues, the germinal epithelium and its derivatives, the medullary cord, rete ovarii, the follicular epithelium, the ova, corpora lutea, atresic corpora and the interstitial cells.

The theories of the origin of cystadenomata center chiefly around wolffian remnants and germinal epithelium. They are of interest not only to explain the cystadenoma but also to account for the carcinoma which may arise from them.

Olshausen, in 1877, and subsequently Fischel, Coblentz, Doran, Howell, and Papov advocated the theory that many of the epithelial tumors, especially the papillary cysts, arose from remnants of the wolffian body. The theory seemed indicated because the great majority of these growths developed in the intraligamentous portion of the ovaries, and the cysts and papillae were lined by cylindrical ciliated epithelium. Indeed, some, as Papov, thought they were able to trace the development of wolffian tubules into cystic cavities which contained papillae. Marchand, in 1878, gave the first real blow to the theory when he described an ovary, the cortex of which was filled with minute cysts containing papillae and lined by ciliated epithelium. Since it was agreed that wolffian body rests were never found in the ovarian cortex, he was forced to seek other origins for the ciliated cells. He advanced the view that the tumors might be derived from the ciliated epithelium of the fimbria of the tube which had extended over the lateral portion of the ovary and had given off tubules of ciliated epithelium, like Pflüger's ducts into the ovarian stroma. From these arose cysts lined by ciliated epithelium. Later Massabuau and Etienne were unable to confirm the observation of Papov. Walthard was able to find only one case of an edematous structure in the wolffian rests in the examination of many ovaries cut in serial sections. Moreover, De Sinety and Mallasez, and later Flaischen, were able to trace the continuity of the germinal epithelium of the surface of the ovary into cysts of the stroma lined by ciliated epithelium. As a result, Olshausen, in 1886, abandoned the theory, since when it has been discarded. Occasionally, it is revived without much supporting evidence. As recently as 1919, Gordon Ley classified papillary cysts and carcinoma as derivatives of wolffian tissues without, however, advancing any proof of origin.

There is considerable evidence to affirm that ovarian cysts can arise from germinal epithelium. Waldeyer first demonstrated their origin from portions of Pflüger's ducts which were remnants either from fetal life or new formed in the adult by the downgrowth of the superficial ovarian epithelium. These observations have since been confirmed by numerous students and recently by Goodall after an extensive study of human and animal ovaries of various age. Bauer also

describes a tumor which arose from downgrowths of the surface epithelium.

Ovarian cysts may arise from the superficial ovarian epithelium as has been demonstrated by Pick and others. Graves, especially, gives convincing proof in two instances that papillary serous cystadenoma may arise from this layer. One growth was inverting and the other was everting, and both were traced to the germinal epithelium of the surface and to its inclusions within the stroma. Voigt's case was found to develop from the surface epithelium, although its morphology suggested a follicular origin. De Sinety and Mallasez, and Flaischen, have also described tumors lined by ciliated epithelium which developed from the germinal epithelium of the surface of the ovary. These numerous observations are strengthened by the fact that there are several different types of cells in the germinal epithelium. Walthard recognized ciliated columnar epithelial cells, small masses of cubical cells, and cells of the goblet type in addition to the typical germinal epithelium. Walthard concluded that the atypical cells were misplaced rests, a tenet that is not accepted by all others. Walthard's goblet cells in the germinal epithelium are at present advocated as the origin of pseudomucinous cystadenoma. All do not agree, however. Pfannenstiel believes that they develop from the follicle.

Pseudomucinous Cystadenoma.—The great majority of ovarian cysts are said to belong to this group, although all students do not agree. Pfannenstiel states that they form two-thirds of the ovarian cystoma, but Graves, in his recent text, states that they were slightly less frequent than the serous growths in his series. They may occur at any time from puberty to advanced age, but are more common between the ages of thirty and forty-five years. It is generally believed that they occur more frequently in unmarried and sterile women.

The tumors vary greatly in size and structure and may attain most extraordinary dimensions. The largest tumor of which we have found record was estimated by Spohn to weigh 328 pounds. Barlowe's tumor weighed 298 pounds and there are 8 others which we have found to weigh more than 200 pounds. We have reviewed this subject in the chapter on mammoth ovarian tumors (page 403). The cysts usually occupy most of the substance of the ovary, although a small part of that organ is generally spread out on one small portion of the surface of the tumor. The cystadenomata are sometimes quite small, and may occasionally push their way into the ovarian and broad ligaments.

The tumor is usually unilateral and appears as a rounded or oval mass covered by a smooth, glistening, pearly gray capsule. It often contains irregular bosses and presents distinct globules. Large blood vessels are rarely seen on the surface. The cyst is usually fluctuant, especially when there is one large compartment. They are generally pedunculated and the pedicle is composed of broad ligament, fallopian

tube, and ovarian ligament. In about 10 per cent of cases, they present as intraligamentous growths. Both ovaries are involved in from 15 to 20 per cent of cases.

The tumors are always multilocular and are composed of numerous cysts. The smaller the tumor, the more uniform size are the cysts. The larger tumors usually contain a few cysts of very large size, which have developed at the expense of the smaller ones which are compressed in the tumor wall. Pressure of neighboring cysts upon the



FIG. 69.—MULTILOCULAR PSEUDOMUCINOUS CYST OF OVARY THE SIZE OF A SIX MONTHS PREGNANCY,

partition wall, which separates them, often ruptures it. Occasionally, smaller cysts project into larger ones and, by rapid growth, tend to obliterate the cavity. Sometimes a large part of the tumor mass is composed of a fine, honeycombed meshwork of glands and minute cysts which, at first sight, suggests malignant degeneration. Expression of the cyst contents shows that the inner walls are smooth and present the picture of a simple cystic adenoma. Yet, scanty low papillary nodules may project into the cavity. In one group of cases, the *papillary pseudomucinous cystadenoma*, the projections are well developed.

The surface of the cyst is usually remarkably free from adhesions. Frequently there are large, dense, fibrous plaques upon the outer surface, and, occasionally, areas of calcification. On cut section, the cyst wall is found to consist of firm, fibrous tissue, usually 4 or 5 millimeters in thickness. The intercystic septa are generally delicate and transparent and are lined with a smooth and glistening membrane. They are sometimes studded with minute granular elevations, yet definite papillary ingrowths are not often noted. A fine crystalline deposit is often present on the inner surface as well as pigmented areas which have resulted from minute hemorrhage.

MICROSCOPIC STRUCTURE.—The outer surface of the tumor is covered with low cubical or flattened epithelium derived from the germinal layer. The cyst wall consists of fibrous tissue arranged in two or three parallel layers. The outer layers are distinctly fibrous and contain few cellular elements, but, toward the inner surface, there are many oval and fusiform cells which present in some places the appearance of normal ovarian stroma. Smooth muscle fibers may be found near the pedicle. In the vicinity of the hilus, young follicles, corpora lutea, and fibrous bodies usually can be seen.

The inner wall of the cyst is covered with cylindric cells which vary in height according to the amount of pressure upon them. The nuclei are small and basal, and the cytoplasm is clear and transparent. They resemble mucous cells, and goblet cells may be abundant. Papillary outgrowths are very rare. They vary in shape but are usually warty and dendriform. The connective tissue stroma of these projections is usually thin and vascular but may be dense and firm. Rarely it appears myxomatous.

Degenerative processes are not uncommon. Fatty degeneration may occur, especially in the epithelial lining, but may be present in the walls of the septa. Areas of calcification are especially apt to be seen when the nutrition of the tumor has been affected by a slow torsion of the pedicle. Atheromatous changes are sometimes found and infarcts are not uncommon.

The contents of the cysts vary considerably, although they are generally ropy and gelatinous. The fluid in the larger cysts is usually thinner than in the smaller cavities. It may be so tenacious in the latter that it can be expressed only with difficulty. Remnants of the partition walls which have been broken down from pressure may be present in the secretion, appearing as masses of fibrous tissue. When they have degenerated, they may show only as whitish lines running through the gelatinous fluid. Sometimes altered blood may be found in the fluid; rarely pus may be present also. The specific gravity varies from 1.010 to 1.030.

The chemical reaction may be either neutral or alkaline. The solids consist of proteid, fats and salts and constitute from one-tenth to one-twentieth of the contents of the cyst. Pseudomucin is the characteristic content of the tumor. It is a glycoproteid which differs from

mucin in that it is not precipitated by acetic acid. In its pure state, it has a clear, glassy transparency. It is most abundant in the small cysts with colloid contents. The color may be considerably altered by transudates which occur from the blood vessels as the result of torsion and by necrotic changes in the cyst wall. Thus, the color may range from white to yellowish, or greenish gray, or even to a dusty brown or black color. The greenish yellow color is due to cholesterin which gives it a shimmering hue. The darker colors are due to altered blood. Microscopically, we find no pathognomonic cells. There may be more or less degenerated epithelial cells, leukocytes, or granular masses of pigment, blood corpuscles or cholesterin plates. Sodium chlorid is the most abundant salt, but alkaline and earthy phosphates may be present. Cholesterin, lucin, urea, cystin and allantoin have also been demonstrated.

The tumor is not often subject to *malignant degeneration*. Carcinomata have been found in only one and a half to two per cent of cases, usually developing in the scar of the stump from which the cyst has been removed. It generally leads to death in from two to three years. The other ovary develops the disease in about 2 per cent of cases.

Solid Adenomata.—This type is not a distinct pathological entity, since, while macroscopically solid, they are in reality pseudomucinous cystadenomata. They constitute about 3 per cent of the cystadenomata. Minute examination shows that they are parvilocular, pseudomucinous cystadenomata presenting a fine honeycombed texture of minute cysts filled with a firm pseudomucinous secretion. They are far more cellular than the ordinary cystic growth and the epithelium is usually atypical, granular and over-nourished. There are many transitional types between this adenoma and the solid and cystic adeno-carcinomata, yet solid adenomata may attain large size without presenting malignant changes. The tumors are usually accompanied by ascites.

Cystadenoma Serosum.—The majority of observers state that the serous cysts are less common than the pseudomucinous. Webster says that they occur only one-eighth as frequently. Ewing claims they are found one-half as frequently, while in Graves' series, they are slightly more numerous.

They usually do not attain the large size of the pseudomucinous tumors, and form swellings rarely exceeding 25 to 30 centimeters in diameter. Most of the serous ovarian cysts are papillary cystadenoma. About one-half of the papillary forms are intraligamentous growths. Often they develop entirely subserously so that, when they attain large size, the peritoneum may be displaced far upward and the neighboring organs pushed aside. The majority of all the serous growths, however, are pedunculated and intraperitoneal.

Externally, the serous cysts closely resemble the pseudomucinous variety. They are also multilocular, although the component cysts are

fewer in number than in the pseudomucinous type. In more than one-third of cases, they appear macroscopically as unilocular growths, yet evidence of daughter cysts may be obtained by microscopic study. The tumors are often bilateral and it is said that 60 per cent of the actively growing papillary forms affect both ovaries, either as primary tumors, or through implantations. The process may not be contemporaneous, however, a fact which must be kept in mind by the surgeon.

Most of the serous cystadenomata show papillary outgrowths of the lining epithelium, which may appear both in the inner lining of the cyst spaces, or upon the outer surface of the tumor. The latter



FIG. 70.—PAPILLARY SEROUS CYST-ADENOMA. Showing cauliflower masses which had not broken through the capsule.

may arise by perforation of the cyst wall and evagination of the growth, or by independent growth upon the outer surface of the tumor. In about 10 per cent of cases, the growth consists entirely of surface papilloma. These tumors are rarely larger than the size of a fist.

The papillary processes vary in form. They may present as warty excrescences or as dendriform branchings arising from a pedicle. They vary in color from white to red and often contain calcareous deposits which may be concentrically arranged (psammoma). The papillary processes are usually relatively few in the larger tumors, yet small cysts are quite likely to be entirely filled with them. The stroma of the papillae consists of vascular, delicate connective tissue, surmounted

by cuboid or columnar epithelium, which is often ciliated. The nuclei are large and densely staining. Serum is often present in the basal connective tissues. The blood vessels are subject to hyaline degeneration.

As the papilloma grow, the epithelial cells rapidly hypertrophy and present irregular proliferations upon the connective tissue stalk. As a result, they form secondary papillae, giving the wall a honeycombed appearance, so that sections of compact papillae may present a glandular appearance.

The cyst contents are originally yellowish, alkaline, serous fluid, rich in albumin, but free from pseudomucin. Later, it may contain increasing traces of pseudomucin, epithelial detritus, fatty substances, and often much blood from the rupture of the delicate vascular papillae.

The papillary growths in the interior of the cysts may perforate their walls and extend into neighboring cavities and also the outer cyst wall, and appear on the peritoneal surface of the tumor. In event of the latter complication, the papillary processes may fasten the tumor to the adjacent organs, as the uterus, rectum, bladder, and pelvic floor. If the rupture has occurred into the free peritoneal cavity, the growth usually becomes quickly disseminated by the formation of so-called implantation metastases. Sometimes these implantations do not develop until some years after rupture, although the ascitic fluid contained detached papillary fragments. Ascites is a regular accompaniment of secondary implantations.

In a small proportion of cases, the metastases disappear after extirpation of the primary tumor, proof of which has been obtained by subsequent laparotomy. Pfannenstiël collected a dozen such cases from the literature. The anatomical process in each case was the same—the papillary nodules flattened out, became transformed into white spots and radiating scars, and finally disappeared entirely, apparently by a reactive peritonitis.

Yet this favorable termination is not to be expected, since the implantations are far more likely to survive on a low grade of nutrition for a long time, and suddenly assume active growth and extend over much of the peritoneum. Adhesions and ascites are invariable accompaniments. The process may last for many years and may be attended by a progressive anemia and emaciation. The peritoneum finally becomes so altered that there is grave disturbance of the intestinal functions. Death finally occurs from cachexia or intercurrent disease.

Thus it will be seen that these tumors lie at the border line of malignancy. Although not causing local destruction of neighboring tissues, or metastasizing through blood or lymph vessels, they extend by direct contact. Indeed, some, as Pfannenstiël, claim that 50 per cent of these cases are really malignant. Later observers do not support this view.

Papillary cysts early give rise to symptoms when they are interligamentary or if accompanied by ascites.

They should be removed through the abdominal route without puncture of the cyst in order to limit the chance of implantations. The opposite ovary should be carefully inspected to ascertain its condition. If cystic, it should be removed together with the uterus.

The tumor may recur after operation in the form of papillary nodules about the stump, in the abdominal wound, or on the peritoneum. Recurrences are seldom, unless the tumor has broken through its capsule. The majority of recurrences follow the removal of intraligamentous growths which have presented technical difficulties. Recurrences have been observed as late as twelve years.

Pfannenstiël states that 77 per cent remain cured five years after removal, yet the period of observation should not end at this time because of the likelihood of even later recurrence.

In direct contrast to the papillary forms, the simple serous adenomata are clinically benign. They grow very slowly, are usually unilateral, cause no metastases and do not recur after operation. Symptoms are unusual, except after torsion, since they are rarely intraligamentous and do not cause ascites.

Racemose Ovarian Cysts.—This rare type of cystic ovarian tumor was first described by Koeberle in 1871. It is seldom seen, since Jayle and Bender, in 1903, were able to find but 17 cases reported in the literature when reporting their case. It is often termed grapelike cystoma, since it is a multilocular tumor, consisting of a mass of vesicles loosely united, some arising from pedicles given off from others springing from the ovary, or from supernumerary ovaries contained in the broad ligament. The mass suggests an atypical hydatidiform mole, although the vesicles vary greatly in size. The largest vesicle in a case reported by Hellier and Smith contained more than 200 cubic centimeters of fluid, while others held only a few cubic centimeters. The wall of each vessel is usually thin and somewhat translucent. It is lined by a single layer of cells, which may be columnar, cubic, or flattened. The columnar cells are generally ciliated. The fluid content is limpid and yellow, and contains a trace of albumin and chlorids. They are supposed to develop from the germinal epithelium of the surface of the ovary.

Myxomatous Degeneration of Surface Papillae.—This form is rather more common than the preceding. It presents as a grapelike growth which is believed to arise from myxomatous degeneration of superficial papillae of papillary cystadenomata of the surface of the ovary. The tumors are not true cysts, since they are composed of myxomatous stroma elements covered with surface epithelium derived from the covering of the ovary. They are easily detached from the main tumor, when they float free in the ascitic fluid which usually

accompanies them. They may give rise to peritoneal implantations. Fritsch reoperated a case twenty years after removal of the primary tumor, and similar observations have been recorded by others. Schroeder reported a case which underwent carcinomatous degeneration.

Other Adenomata.—The superficial or everting papillary adenoma may also present as a solid tumor. Small growths are fairly common, although large ones are rare. The growth is essentially benign, since many cases have been extirpated without recurrence.

Adenofibromata have also been described. They usually present scattered glandlike formations in the substance of the fibromatous tumor. These are believed to arise from invagination of germinal epithelium. Inclusions resembling endometrium have been described by Pick, Pfannenstiel, Russell, and, quite recently by Norris.

Epithelial alveoli are occasionally seen in true ovarian fibromata. They may undergo a cystic dilatation and subsequent carcinomatous change.

OVARIAN CARCINOMA

It is rather difficult to determine the frequency of true ovarian carcinoma, since many of the statistics are incomplete, and others include the malignant degenerations of ovarian tumors that are ordinarily benign. Schmidlechner, of Budapest, records 720 ovariectomies done in a series of 50,000 gynecologic patients between 1880 and 1904. Of these, 147 were done for malignant tumors. Sixty proved to be adenocystomata that had undergone malignant changes; 52 were primary carcinomata. Ewing, combining Martin's and Libbert's statistics, states that 22 per cent of more than 200 cases of ovarian tumors were carcinomatous.

Etiology.—The etiology is not known. Carcinomata develop from epithelial elements in the ovary, yet we do not know which group of cells is more likely to be altered. The earlier theories attempted to correlate carcinomata with the lining of the graafian follicle because the histologic features of some of the ovarian cancers appeared to reproduce both the primordial and growing graafian follicles. This theory was first advanced by Accorici in 1890 and has later had the support of Emanuel, von Kahlden, Pozzi, Beassenat, Gottschalk, Schroeder and Delepine. Others, however, urge that since the ovules and primordial follicles are formed during embryonic life, it is not likely that their features could be reproduced even by a pathologic process at a later period. A large number of the more recent authors, including Voigt, Pollano, Blau and Ingier, believe the structures which resemble primordial follicles in the folliculoma group of cancers are, in reality, degenerative processes in the center of the carcinomatous alveolus about which the surrounding epi-

thelium presents a radial arrangement. Although some ovarian cancers may contain alveoli which closely resemble a graafian follicle, similar structures have been described in carcinoma in other organs, as has been demonstrated by Lipmann. There remains, therefore, the possibility that cancers may arise from Pflüger's tubes, germinal epithelial rests as claimed by Walthard, müllerian structures, or from invaginations of the germinal epithelium, a view which, at the present time, is favored by many laboratory workers.

The studies of histogenesis indicate that developmental anomalies are probably responsible for the majority of the tumors, since other predisposing factors do not appear likely. Trauma, which is often considered important in tumors of the exposed surfaces, cannot be a factor because of the protected position of the ovaries. Inflammatory changes are probably not of much importance, since Massabuau and Etienne could obtain a history of an inflammatory condition in only 10 of 250 cases. The influence of heredity has not been proved, since it was demonstrated in only 6 cases of the same series. Proper family histories, however, are very difficult to obtain. The patient's occupation did not seem to be of importance. Heinrich claimed that ovarian cancers usually occurred in married women, whereas the benign tumors were more likely to occur in the unmarried. This observation has not been confirmed. Massabuau and Etienne tabulated their cases to determine whether pregnancy was a factor but were unable to reach definite conclusions. Excluding the cases which were too young to have had children, they found that 97 had been pregnant, whereas 26 had not. Nine cases had had only one child while the others had had several. One case had had 11 children. Eleven cases had had abortions, one having had 3. All the pregnancies had been normal except one which had had hydramnios. Only 1 case had had an instrumental delivery. The pregnancies very often antedated by many years the development of the cancer.

Age.—Cancers of the ovary have been observed at various ages ranging from four to sixty-nine years, although the great majority occur between the fourth and sixth decades. Olshausen claimed that carcinoma developed very frequently in very young children, yet others state that the majority of these cases are sarcoma. Massabuau and Etienne collected 13 cases occurring before puberty, 69 cases during active menstrual life, and 38 cases after the menopause. The Krukenberg tumors occur fairly early, since the majority are observed during the third decade. Scirrhus cancers are most frequent after sixty, and may develop so insidiously that they are first discovered at post mortem.

Classification.—There is considerable difficulty in classifying ovarian carcinoma, because of the large number of atypical growths that do not fit readily into any grouping. The great majority of ovarian tumors are primary in the ovary. A very large proportion of these arise *de novo* from apparently normal organs. The larger number, however, result from car-

cinomatous changes in growths which were originally benign. The older authors attempted the division of all of the ovarian cancers into solid and cystic carcinomata. This has not proved satisfactory, because of the frequency with which large cellular growths, originally solid, break down and undergo cystic changes. There are also a number of cancers which merit special consideration because of distinctive features of growth or etiology. Thus, in addition to the solid and cystic ovarian cancers, we should consider the folliculoma malignum, the squamous cell carcinoma, the clear cell cancer, the carcinoma mucocellulare of Krukenberg, and other and presumably metastatic cancers.

Solid Ovarian Carcinoma.—This group forms about 15 per cent of ovarian cancers. They may be primary growths, yet are often metastatic. They may be subdivided, according to their morphology, into two groups: (1) the alveolar or medullary carcinoma, characterized by its alveolar structure, soft consistency and scanty fibrous tissue stroma; and (2) the scirrhous tumor which is dense and fibrous and contains a relatively small amount of epithelial cells. The genuine, or idiopathic, carcinoma of Gebhard forms the majority of the medullary carcinoma. While originally solid, the larger medullary growths are likely to present late in their development cystic areas which result from degeneration.

The size of these tumors varies between rather wide limits, although they are usually small and seldom exceed an infant's head in dimensions. They may, however, develop into very large growths. Massabuau and Etienne record one which was as large as a uterus at term and weighed 6 kilograms. The largest tumor of which we find record is Gebhard's, weighing 7,300 grams.

The tumors are at first unilateral, yet the second ovary has become involved in nearly 50 per cent of cases by the time the case comes to operation. They are usually pedunculated and lie at first in the pelvis to arise subsequently into the lower abdomen. Originally free, the growth later becomes fixed by adhesions of inflammatory or neoplastic origin. The pedicle is usually short and torsion is not common. The growth seldom develops within the broad ligament. Massabuau and Etienne found only 14 such cases in 250 carcinoma. Strange to say, Schmidlechner's series of 33 cases contained 9 of these, while the other 5 were scattered among the remaining 217.

The solid tumors are usually irregularly rounded in form. They are seldom spherical. Early growths may retain the shape of the normal ovary. Sometimes the tumor mass may be divided into distinct lobules by deep furrows. The surface of the tumor is grayish pink in color, and, in its early stages, is smooth and without adhesion formation. Large flat veins may be seen beneath the surface of larger tumors. Later in its development, the growth breaks through the capsule and presents yellow translucent cancerous masses, or a softer brainlike substance which oozes out between the connective tissue fibers.

The outer capsule is derived from the tunica albuginea. It consists of a connective tissue membrane averaging 4 or 5 millimeters in thickness. On gross section, the tumor appears homogeneous and of a yellow gray color, yet careful examination shows pea- to egg-sized cancerous areas in the midst of rather edematous connective tissue fibers. There may be small cysts, in the larger of these areas which contain yellow fluid discolored by hemorrhage. They are lined by an irregular wall of soft, friable tissue, suggesting that the cysts arise by necrosis and liquefaction. Rarely there are true cysts lined by epithelium lying near the surface of



FIG. 71.—SOLID OVARIAN CANCER, SCIRRHOUS TYPE. Developing in ovary following supra-vaginal hysterectomy for uterine fibroids.

the tumor. The tumor itself may be mottled by hemorrhage so that it gives an appearance like marble.

Morphologically, there are a confusing variety of forms, yet the majority of the cancers present an alveolar type. The cancer cells are arranged in small, solid cords, usually without definite lumen, lying in a fine, delicate, connective tissue stroma. The outlines of the alveoli cannot be determined in all sections and the growth may strongly suggest a round cell sarcoma, yet examination of other slides discloses the true nature of the tumor. The cancer cells are polygonal in type, but when rapidly growing may be quite irregular.

In one type of growth, the cell masses are arranged like tubules.

The pure medullary type has large broad columns which frequently anastomose and which are composed of small polyhedral, or rounded, opaque, granular cells. The connective tissue stroma is scanty and has few small nuclei.



FIG. 72.—SOLID OVARIAN CARCINOMA, MEDULLARY TYPE. Macroscopically the tumor suggested a hemorrhagic follicle cyst. The tube and ovary were removed. The patient remains well after four years.

A rather rare variety of medullary carcinoma has many large, clear cells which resemble ova. They are scattered through the tumor at extremely regular intervals and bear a striking resemblance to young developing follicles. Occasionally, the whole tumor seems to be composed of myriads of slightly dilated normal follicles. Emanuel believed that these cases developed from malignant changes in primordial ova, yet this view is not accepted by most recent observers. The cells strongly suggest cross

sections of mucinous stroma and the majority ascribe such an origin to the tumor.

The scirrhus type present only fine strands of epithelium in a comparatively dense, fibrillated stroma. The epithelium is arranged in single or double rows of cells and occasionally in small nests or glandlike structures. Some, as Orthmann, believe that they may arise from degenerations of the downgrowth of germinal epithelium into ovarian fibroids. They may also arise from carcinomatous change in the glandular epithelium of fibroadenoma. The majority of scirrhus growths are not primary but are metastatic tumors. They are usually bilateral.



FIG. 73.—SOLID OVARIAN CARCINOMA, MEDULLARY TYPE. On section of the tumor (Fig. 72), a hemorrhagic mass escaped consisting largely of cancerous tissue.

Cystic Carcinoma.—Cystic carcinoma may develop as a primary process in which the cysts are produced by the secretions of the cancerous cells; or as secondary changes in cystic tumors that were primarily benign. They may also result from degenerative changes in the solid cancerous tumors.

The cystic adenocarcinoma may be divided into two types corresponding to the two types of benign cystadenoma, i.e., adenocarcinoma papillare, and adenocarcinoma pseudomucinosum. The former is far more common.

The adenocarcinomata papillare form a most interesting group. They reproduce in gross structure the essential features of the papillary cystad-

enoma. Some indeed, as Pfannenstiel, believe that cancerous changes may be found in nearly 50 per cent of the tumors which are ordinarily classed as benign, a point not conceded by Gebhard and many other later students.

In their macroscopic appearance, the carcinomatous papillomata resemble the serous cystadenomata, yet, as a general rule, the malignant areas may be easily recognized by the naked eye. The tumors rarely attain the size of the large cystadenoma and are seldom larger than 10 or 15 centimeters in diameter. Some are pedunculated and freely movable, yet the larger number is either intraligamentous or pedunculated growths which have been firmly bound down by adhesions. The capsule of the larger growths is usually perforated and covered by papillary outgrowths which have developed from the substance of the tumor. The cancer cells have invaded the neighboring peritoneum. The tumors are usually bilateral, yet one side is often histologically benign, while the other side is frankly carcinomatous. Especially interesting is the development of malignancy in an ovary which appeared perfectly normal at the time its fellow was removed because it was cancerous.

The papillary outgrowths in the malignant cyst at first sight appear to exactly resemble those of the benign cysts. Careful macroscopic examination, however, reveals the cellular structure and their true character. Pressure with a scalpel allows the expression of the milky cancer juice. In other cases, the papillary structure is scarcely visible because of the atypical growth of the cells. Minute cysts may be present in the walls, having arisen from seemingly solid nodules which sprang from proliferation of the cells of the papillary processes. When an apparently benign cyst is becoming malignant, the cancerous processes will be surrounded by others which are seemingly benign.

The solid surface papilloma may also undergo carcinomatous degeneration and become transformed into typical adenocarcinomatous masses.

The contents of the small cysts are clear, serous fluid. The larger cysts contain turbid material from desquamated epithelium. They may be discolored by hemorrhage.

Microscopically, these tumors present the typical features of adenocarcinoma, often showing a very close resemblance to the adenocarcinoma of the uterine body. The multiplication of cell layers, cohesion of adjoining papillae, the filling of intermediate spaces and pseudo-alveoli with atypical cells, are usually features of malignancy, in addition to the basic elements of invasive characteristics and evidence of rapid cellular reproduction.

Not all tumors assume this typical form and mixed types are very common. The growths may be composed of nonglandular, solid medullary masses, containing very small cystic spaces in the connective tissue framework. The cysts are lined by a many-layered polymorphic epithelial cell. The stroma of these growths varies greatly. Occasionally, it is very cellular and may even resemble sarcoma. Calcification may occur in either the con-

nective tissue stroma or the epithelial masses. It is likely to be laid down as concentrically layered psammoma bodies.

The metastases are usually local as in the adenomata. They also are implantation metastases but are aggressive and never spontaneously disappear. They spread by direct extension, even through the diaphragm and through the pleura. They are accompanied by serous effusions. Intraligamentary growths less frequently produce ascites. Extensions from them fairly permeate the neighboring organs. Lymphatic or bloodstream metastases are extremely rare.

Adenocarcinoma Pseudomucinosum.—These tumors are seen very rarely. A few are probably malignant from their inception, while the majority develop because of malignant changes in the originally benign cyst. In the same way, implantations or recurrences from a tumor benign in its own structure may develop in the peritoneum, the operative stump, the abdominal scar and suddenly assume a carcinomatous form. Very rarely, the pseudomucinoma peritonei may develop malignancy.

In the pseudomucinous tumor, also, the malignant degeneration may appear as papillary excrescences, yet is more likely to present as a proliferation of the epithelial lining of the small cysts which becomes many layered and shows marked changes in cell type. The cells increase in number and height, lose most of their ability to secrete mucus, and become granular and opaque, with large nuclei containing abundant chromatin. Occasionally, the walls of the larger cysts are transformed into thick cancer masses. Rarely the growth is more diffuse and obscures the glandular structure.

Macroscopically, the cancerous areas appear very cellular and friable. While they are not easily distinguished with the naked eye from benign tissue composed of closely packed minute cysts of microscopic size, they may be readily differentiated by the microscope. The large cystic spaces are usually preformed but may arise by necrosis of cellular cancerous areas. The latter type usually contain hemorrhages. The true cysts have very little mucous secretion. The smaller alveoli have more. The cyst fluid is usually turbid from epithelial debris and discolored by blood. The tumor's capsule is often perforated and presents a cancerous growth upon its outer surface. The mass is bound down by adhesions and surrounded by implantations. Metastases in the regional lymphatics are common. Distant metastases are rarely seen.

Folliculoma Malignum.—This is an atypical alveolar carcinoma which suggests thyroid tissue. It was first described by Gottschalk in 1899. There is not yet complete agreement as to its origin. Gottschalk believed that it originated from the follicle and was comparable to the benign graafian follicle adenoma described by von Kahlden. Pick claims that it is a carcinomatous degeneration of an ovarian struma of teratomatous origin in which the other teratomatous elements have been suppressed. Both Voigt and Bauer proved that their cases developed from the germinal epithelium.

Gottschalk's tumor was a fist-sized, grayish white, unilateral growth which had involved the left ovary of a woman of forty-eight. There was marked ascites but no metastases could be demonstrated. The cut surface showed numerous minute cysts, particularly in the cortex of the tumor. The tumor was very vascular and showed areas of interstitial hemorrhage. The stroma was not cellular and contained areas of hyaline degeneration. The parenchyma consisted of sheets of protoplasm without definite cell boundaries, suggesting thyroid tissue. The small cysts in the center of the masses contained mucinous material and resulted from cell degeneration. The microscopic structure resembled struma ovarii which may form a component part of ovarian teratoma. Gottschalk recognized the resemblance but ruled out struma, because there were no other teratomatous elements, and also because the areas suggesting thyroid were not primary features of the tumor but were the result of secondary cystic degeneration.

No growth yet described has contained iodine.

Somewhat similar to the so-called folliculoma malignum are the *granulosa cell carcinoma* described by Werdt and the *oöphorim folliculare* described by Brenner. Both of these tumors gave rise to multiple small cysts in an enlarged ovary.

Primary Squamous Cell Epithelioma.—Primary squamous cell epithelioma was described by von Hausemann. He believed that it developed from a metaplasia of ovarian epithelium, or possibly from squamous epithelial rests which were described by Walthard. An ovulogenetic origin is not probable, since there were no other teratomatous elements in the ovary.

Atypical Forms.—There are a number of types of ovarian cancer which are not clear cut.

The first group present features which suggest an endothelial origin. Probably many of the so-called ovarian endothelioma really belong in this group. The cancers are alveolar and the indistinct alveoli are formed by unusually small cells. The alveoli vary greatly in size. The cells may be arranged about blood vessels, or there may be areas of diffuse growth where the epithelium is intimately mingled with the stroma or appears in rows between the stroma fibers. In another group, also described as endothelioma, the cell masses are large, circular on section, and composed of large polyhedral, clear or slightly granular cells.

The Clear Cell Cancer.—This tumor was first described by Chenot, in 1911. More recently, Horand and Fayol have described a case arising in an accessory ovary. It is also an alveolar cancer.

The connective tissue fibers which separate the alveoli are thin and delicate and from them are given off very fine fibrils which extend into the alveoli and envelop the cells with a very fine reticulum.

The alveoli are composed of cells which are very different from the ordinary typical carcinoma cell. They are large and irregularly polygonal. The nucleus is central, round or oval, sometimes kidney-shaped, vesicular

and clear. The chromatin filament is very delicate with small, well-stained nodules which give it a finely punctuate appearance. The protoplasm is extremely clear and shows a zone of condensation just next to the nucleus in which are one or two deeply stained centrosomes. The protoplasm appears reticulated with clear vacuoles which contain glycogen. The limiting membrane is well marked.

Chenot considered his growth identical in type and histogenesis with the testicular tumors described by Chevassu as "seminomata," and believes that both are derived from the germinal epithelium. He considers their morphologic and staining similarities absolutely identical. Massabuau and Etienne, however, find certain differences in the morphology and call attention to the fact that such clear-celled cancers are not found exclusively in the ovary or testicle, and hence are not necessarily derivatives of germinal epithelium. They describe similar tumors in the kidneys and mammary glands and ascribe the clear appearance of the cell to some chemical change and especially to a large amount of glycogen.

Carcinoma Resembling Lymphosarcoma.—There is a solid ovarian carcinoma which presents a diffuse growth of small round cells and resembles lymphosarcoma. It occurs in young subjects, is bilateral, of rapid growth, and produces widespread local extensions and numerous bulky metastases. Stone's case presented metastases from the breast.

Krukenberg Tumor.—This interesting tumor was first described by Krukenberg in 1896. He reported 4 cases and collected from the previous literature a number of similar cases which had been described under various names. The tumor has fairly definite characteristics. It was bilateral in 39 of 43 cases collected by Major in which the data was complete. The age varies. Chapman, in 1920, observed the growth in a girl of fourteen. The average age of Major's series was thirty-six years. The tumor develops slowly and is accompanied by ascites, often chylous in nature. It usually preserves the outline of the ovary, although the surface may be nodular, and is firm in consistency, especially in the periphery. The center often presents soft, myxomatous areas. There may be large areas of cystic degeneration and, occasionally, small cysts lined with epithelium which appear like dilated follicles. The firm part of the tumor consists of spindle-shaped cells, suggesting proliferated ovarian stroma. In the myxomatous areas, the cells are large and round, appear swollen by mucoid degeneration with a nucleus pushed to one side in the very boundary of its capsule.

These tumors often remain stationary for a long time but tend to spread through the lymph channels, at first within the ovary, later into the broad ligament and tube, and, occasionally, to give widespread metastases through the body. Death resulted in all of the cases of Major's series in which the outcome was known.

The cells filling the lymph vessels are markedly swollen and may occlude the lumen. Krukenberg believed that they were degenerated stroma cells,

because he could not demonstrate a connection between them and any of the epithelial elements of the ovary. They present like mucous cells. He called the tumor fibrosarcoma mucocellulare carcinomatodes.

The growth was believed by Krukenberg to be primarily of ovarian origin, yet it is now known that it is usually secondary to stomach carcinoma. It is well known that ovarian tumors which arise secondarily from primary carcinoma within the abdomen attain such size that presently they control the clinical picture. Schlagenhauser, in 1902, added 4 cases and Major, in 1918, collected 55 cases as well as 8 others which he felt should be included in the group. Whether the tumor may ever be primary is still a matter of discussion. Major found 5 cases in which no primary tumor of the stomach or intestines was observed at autopsy (cases of Krukenberg, Glockner, Schenk, von Rosthorn, and Sternberg).

Metastatic Carcinoma.—Until quite recently, the ovary was supposed to accord with Virchow's diction that organs which showed a decided tendency to primary tumor formation rarely were the seat of metastatic growths. Rokitansky and Billroth described metastatic ovarian tumors but considered that they were very rare. Others, as Pfannenstiel, thought that ovarian carcinomata, when present with cancers of the gastro-intestinal tract, were in reality independent primary tumors. The first decided advance came when Bucher collected 9 cases of ovarian cancer, 4 of which were associated with carcinoma of the stomach, and 5 with carcinoma of the breast. Bucher regarded the ovarian tumor as a secondary growth in all instances. Similar case reports presently appeared in the literature by Walter, Bode, Fleischmann, and others, so that Gebhard stated in his text that metastatic ovarian carcinoma was probably more frequent than had previously been recognized. Heinrichs emphasized the need of carefully exploring the entire abdomen when operating for ovarian tumors to diminish the chance of overlooking a primary growth.

Schlagenhauser, in 1902, was the first to make a careful review of the literature from which he collected 79 cases, including 8 of his own. The ovary was associated with stomach tumors in 61 cases, the intestinal tract in 10, the bile tract in 7, and the supra-adrenal gland in 1. Schlagenhauser thought that all of the primary growths were carcinomata, although some had been reported as atypical cancers. The ovarian growths were variously diagnosed as carcinoma, endothelioma, sarcomatoma, adenoma, Krukenberg tumor, myofibroma, etc., although they reproduced more or less closely the type of tumor in the other part of the abdomen, with such variations as could be accounted for by the difference in the host. He thought that many of the ovarian growths reported as endothelioma and sarcoma were in reality metastases from scirrhus gastric carcinoma. While the subject has not been finally settled, it seems likely that so great an association of primary tumors in the abdomen would be at least most unusual. Gastric carcinoma is usually primary; very rarely secondary. The fact that the ovarian cancers in Schlagenhauser's review were nearly always bilateral, and occurred

in women whose ovaries were still functioning, seems to indicate that these growths may well be secondary.

The metastases frequently dominate the clinical picture. The gastric carcinoma may be latent and, even when suspected, may not be found until post mortem. In many of the cases collected by Schlagenhauer, insufficient attention was paid to definite gastro-intestinal symptoms before operation. In only 5 of the 79 cases was the primary operation directed toward the upper abdominal tumor. Bland Sutton, later, found ovarian carcinoma in 10 per cent of autopsy cases with mammary or gastric carcinoma. Other series have been reported by Glockner, Stickel, Engelhorn, Amann, and Goulliond.

The association of mammary and ovarian cancer has received less attention. Coupland, in 1876, found ovarian metastases in 6 per cent of 80 mammary carcinoma and Toerek and Wittelshofer found them in 7 per cent of 366 cases. Handley has studied 422 mammary cancers which he divided into two classes, according as they died late in the disease, or earlier from more or less accidental causes. Ovarian metastases were found in 8.6 per cent of the former, and in only 4.8 per cent in the latter group.

Stone, in 1916, reviewed the subject of ovarian metastases and added 133 cases from the literature to the 79 cases collected by Schlagenhauer. The primary tumor was found in the stomach in 75 cases, in the breast in 25, in the large intestine in 22, in the gall-bladder or ducts in 5, in the small intestine 4, and 1 in the pancreas and 1 in the appendix.

Amann, from a study of 18 of his own cases, and a review of the literature, believes that secondary ovarian carcinoma may be grouped into three histological types: (1) the edematous fibroma, with epithelial infiltrations which may show colloid degeneration; (2) the nodular medullary carcinoma; and (3) the cystoma with areas of fibrocarcinoma.

Amann's first group suggests that the ovarian connective tissue hypertrophies tremendously as a characteristic reaction to the invasion of neoplastic elements, since the epithelial alveoli are usually very scanty. There is usually marked edema, or cyst formation, in the central parts of the tumors. Hemorrhagic areas are frequent. The epithelial elements show colloid degeneration and sometimes present as typical colloid carcinoma similar to that seen in the gastro-intestinal tract. As has been already indicated, there is very strong feeling that the Krukenberg tumor really belongs in this group. Four of Amann's cases were Krukenberg's tumors, as were 4 of Schlagenhauer's 79 cases, 4 of Stauder's 60 cases, 2 of Glockner's 15, and 1 each of Wagner's and Schenk's. Primary gastro-intestinal cancers were demonstrated in nearly all of the 63 Krukenberg's tumors reported by Major in 1918. The fact remains, however, that there are 5 cases of Krukenberg tumors in which careful post-mortem examination failed to demonstrate primary tumors of the stomach or intestine. Others of Amann's first group of tumors presented a histologic structure rather similar to endothelioma or sarcoma.

Cyst formation is frequently found in the second group of solid nodular adenocarcinoma in contrast to the third type which are true cystoma with fibro-adenomatous and carcinomatous alveoli. Edema is a common finding in all of the tumor groups.

ROUTE OF METASTASES.—Various methods of extension appear possible. Thus the cells may be transported by lymph or blood stream or by direct implantation of tumor particles through the peritoneal cavity.

The last view is accepted by the majority of more recent authorities who believe that the primary tumor early penetrates the serosa in a microscopic manner. The general peritoneum does not share in the involvement, possibly, as Krauss urges, because the germinal epithelium is more permeable than the peritoneum, a conclusion which is not acceptable to Wolffheim. This author believes the ovary is most susceptible, because of the injury to its surface resulting from rupture of the graafian follicles. The fact that the ovary often lies in the pouch of Douglas is believed by many to favor peritoneal implantation.

Metastases by way of the blood stream probably occur only in exceptional cases.

Mammary carcinoma, according to Handley, spread by the lymphatics through the deep fascial plexus to the epigastric triangle, when the cancer cells invade the peritoneal cavity and follow the same metastatic routes as the intra-abdominal carcinoma.

The metastases may be transported through the lymphatics directly or by a retrograde process. Direct extensions probably occur only when the primary tumor is in neighboring organs, as the rectum or sigmoid. Roemer, Glockner, Stickel, Pfannenstiel, and others, believe that the majority of cases result from retrograde lymphatic transportation. They state that the invasion extends through the lymph vessels and nodes behind the stomach and pancreas into the retroperitoneal lymphatics which lie on both sides of the aorta, to the enlarged lumbar nodes, from which the cells are transported into the ovaries through the hilum by a reverse current in the lymph vessels along the ovarian artery and vein. Oscar Frankl has recently supported this theory in an extensive paper. He calls attention to the fact that there is associated with a very large proportion of metastatic ovarian carcinoma a microscopic invasion of the lymphatics of the uterus and tube. This is found in the musculature or mucosa but rarely on the peritoneal surface. Primary ovarian carcinoma, on the other hand, frequently shows peritoneal implantations on the surface when it metastasizes to the uterus, yet a microscopic involvement of the lymphatics is not seen.

CLINICAL FEATURES OF OVARIAN CANCER

Stages of Growth.—Ovarian cancer may present three stages of growth, local, regional and general. The first stage is marked by enlargement and rapid destruction of the ovary. The steps may not be clearly

defined, however, even in the very early stages, since many tumors originate from surface germinal epithelium when there is, at the same time, local and regional growth. When the tumor remains encapsulated, there may be very little normal ovarian tissue at the end of the first stage. Only one of Massabuau and Etienne's series of 250 cases presented any normal structures.

The second stage is marked by invasion of the regional lymph glands and the neighboring organs. The opposite ovary usually is the first organ involved. Early extensions probably occur by direct invasion through the peritoneal cavity accompanied in their latter stages by lymphatic involvement. Peritoneal implantations may be observed in the latter part of this stage on the large and small intestine and in the pouch of Douglas. They may be noted in cases which do not present adhesions, although this complication is more usual. The adhesions may be of inflammatory or neoplastic origin.

The third stage is marked by a generalization of the carcinomatous process throughout the body. The invasion results from extension into the blood vessels. True peritoneal carcinosis is often noted.

Involvement of Lymph Glands.—The lymph glands are usually involved by the time the case comes to operation. They are invariably involved in the late cases. In 7 of Massabuau and Etienne's cases in which a complete postmortem examination was made, the lumbar glands were involved in 5 cases, in 1 of which one side only was affected. The internal iliac glands were twice involved and the mesenteric glands in a similar number. The subrenal and bronchial glands showed carcinomatous changes in 1 case in which the disease was generalized. The mesenteric glands may be invaded by retrograde metastasis or secondarily from peritoneal implantations on the intestinal wall.

The ovarian lymphatics merit description. They begin as a capillary network about the follicles and drain into five or six trunks which follow the blood vessels, passing in front of the ureter to empty on the left side into a group of two or three glands lying in front of the aorta, and a little below the hilum of the kidney. The glands on the right side lie a little lower down and upon the vena cava. The larger lymphatics contain few valves and allow a retrograde circulation. There are a few small accessory glands along the course of the ovarian vessels. The ovarian lymphatics do not form a closed system but anastomose freely with those of the uterus and vagina and thus come into relation with the hypogastric, external iliac and even with the crural glands.

Involvement of Neighboring Organs.—The tube of the affected side early shows inflammatory changes and later is invaded by the cancer. The adnexa of the opposite side soon become involved and present the same appearance as the primary growth. Even though they appear normal macroscopically, foci of the disease may be demonstrated with a microscope. The uterus may show mechanical, inflammatory, or neoplastic

changes. Primary ovarian carcinoma do not give rise to uterine metastases in their early stages, although the ovary is early invaded by extensions from uterine cancers. Massabuau and Etienne found uterine metastases in only 2 of their 250 cases. The broad ligament is not usually involved, nor is the vagina, except in the very late cases. Omental metastases are common, as are regional peritoneal implantations.

The bladder is not often invaded, although it may be displaced or adherent. Massabuau and Etienne could not demonstrate carcinomatous infiltration in the ureter of any of their cases, even though the kidney in one case showed extensive disease. Metastases may be found in the kidneys, liver, lungs, pleura, and very rarely in the spleen and heart.

Symptoms.—The symptomatology varies. Occasionally there may be no symptoms. The tumor was accidentally discovered in 16 cases in the Massabuau and Etienne series. Patients presenting early growths may complain of pain, menstrual disturbances, or increase in the size of the abdomen, or very rarely disturbances in the general health.

Pain is the most frequent initial symptom and may develop insidiously and gradually increase, or may appear with the suddenness of an acute abdominal crisis. It occurs with equal frequency in the very young and the aged. It is usually in the ovarian region and may be accompanied by pain which radiates to the iliac fossa or down the leg. Occasionally it is only backache which radiates to the groins. Often it is merely a sense of heaviness, yet it may be lancinating and severe.

The menstrual disturbances may consist of amenorrhea, irregularity, or menorrhagia. Massabuau and Etienne found that suppression of the menses constituted the first symptom in 8 cases, in 2 of which it ceased abruptly. Irregularity is more common and may precede either amenorrhea or metrorrhagia. Menorrhagia alone rarely marks the onset of symptoms. Metrorrhagia is far more common and may present in women past the menopause without premonitory symptoms.

Increase in size of the abdomen is usually due to ascites, since the tumor itself plays a secondary rôle. Ascites may be present even when cancerous involvement of the peritoneum cannot be demonstrated. It was present in 35 of the 41 cases in which the condition of the abdomen was recorded in Massabuau and Etienne's series, and absent in 6. The increase in size of the abdomen constituted the first symptom in 28 cases.

Disturbances in the general health, digestive upsets, or urinary symptoms occasionally may constitute the first symptoms of the disease.

The initial symptoms do not long remain as the sole complaint. The patient looks sick, becomes emaciated, has cessation of menstruation, and complains of vomiting and pain. Constipation may be extremely obstinate. Menses cease invariably when both ovaries become

involved. The urinary symptoms include polyuria, imperative micturition, slight incontinence and dysuria. There is usually edema of the legs and back and dyspnea in the stage of cachexia. Some patients have a tendency to somnolence.

Complications.—Complications are rather rare. Torsion of the pedicle is not often seen. Occasionally, ascites may be sufficient to cause pressure symptoms and dyspnea. The fluid soon recurs after tapping. Intestinal obstruction is not unusual in the terminal condition when phlebitis may also be present. There may be anuria.

Pregnancy occasionally forms a complication and abortions sometimes result. Dystocia may occur if the tumor becomes jammed down in the pelvis in advance of the fetal head. The growth increases rapidly during the pregnancy because of the increased vascularity of the pelvic structures.

Diagnosis.—The diagnosis is not often made in early cases, since there are rarely findings other than the presence of an ovarian tumor. Bilateral growths accompanied by gastric disturbances should arouse the suspicion that the condition is metastatic. Yet visceral neoplasms develop frequently without marked symptoms, and the great majority of bilateral ovarian tumors are papillary cystadenomata. In the later stages, the diagnosis is more simple because of the presence of definite symptoms of malignancy. Yet the clinical diagnosis is often incorrect. There is marked ascites, loss of weight, symptoms of intestinal obstruction and the presence of a more or less fixed tumor. Even a histologic diagnosis may be made occasionally only with difficulty.

Treatment.—The treatment is removal of both ovaries, together with the uterus. Theoretically logical, it may be difficult of accomplishment. The presence of adhesions and metastases may complicate the operation. In marked contrast to uterine cancers, operation may be attempted even in late cases of ovarian malignancy, since the mere size of the tumor may give rise to symptoms. Both ovaries should be removed because of the frequency with which cancerous deposits are found microscopically in ovaries which appear normal on casual inspection. The uterus should be removed, since it adds to the chance of cure. Several investigators have developed upon the cadaver a method of removing the lumbar glands, yet this procedure cannot be advised at present, since it may not prove necessary in early cases and will not aid in the later ones. Implantations upon the viscera should be removed when they are distinctly local. If, however, the glands are involved, the procedure will be valueless. Before attempting the removal of ovarian cancer, the upper abdomen should be thoroughly explored to determine whether there is another malignant tumor. This should be treated, if present, as the conditions warrant, yet the removal of secondary ovarian tumors may be warranted if they dominate the

clinical picture. Frankl advises post-operative Roentgenotherapy. Secondary operations for metastases may prolong life occasionally.

Prognosis.—The literature shows that operations have been attended with considerable mortality. Massabuau and Etienne found an immediate mortality of 24 per cent in 49 cases of simple oöphorectomy, 22 per cent in 27 cases of bilateral oöphorectomy, and 9 per cent in 22 cases of hysterectomy with bilateral oöphorectomy. While this represents the mortality of an earlier surgical period, it stands to reason that there will always be definite mortality when patients weakened by ovarian cancer undergo extensive operative procedures. Shock is extremely likely. Adhesions to the small intestines may demand intestinal resection in rare cases and adds to the mortality.

Of 89 operative recoveries, Massabuau and Etienne found that 59 had been followed. Of these, 48 died of recurrence and 11 survived, 7 for more than four years. The value of the statistics is impaired by the fact that the cases were variously treated, some by simple oöphorectomy and others by double oöphorectomy, with and without the removal of the uterus. The tumor may recur after operation in the form of papillary nodules about the stump, in the abdominal wound, or on the peritoneum. The recurrence may not be suspected for some time after removal of the original tumor, even as long as two years. The majority of recurrences follow the removal of intraligamentous growths which have presented technical difficulties. Recurrences have been observed as late as twelve years. These figures supplant the older report of Pfannenstiel. He stated that there were 83.3 per cent recurrences in papillary carcinoma which had been followed for four years as contrasted with 66 per cent for the other types of ovarian cancers which had been under observation for a similar period. There are no other series of size from which we may draw conclusions, yet, since recurrences have been recorded between six weeks and eight years, it is difficult to speak of true cures. The survival following recurrence is usually very short. The patient succumbs to cachexia, and rarely lives longer than six months.

EMBRYOMA

This includes dermoids and the teratoma, both of which arise from germ cell elements and contain all three germinal layers. The dermoids are essentially benign tumors, composed of adult tissues arranged in a more or less orderly manner to represent rudimentary organs. The teratoma, on the contrary, are malignant tumors composed of embryonic cells which are mingled indiscriminately without tendency to orderly arrangement. There are numerous transition forms which occur between the two types of tumors, thus building up an almost continuous series.

Etiology.—Since the same views for the etiology are advanced for both tumors, we will consider them before taking up their clinical manifestations. Two views are now advocated: (1) that they develop from an unfertilized ovum; and (2) from an isolated somatic blastomere, which by some irregularity of development has been included in the ovary. The theory that they develop from mature ova which were impregnated before they left the graafian follicle no longer holds. Such a phenomenon would result in ovarian gestation rather than a teratoma. It would not explain the tumor in unborn fetuses and infants. Tumors at this age cannot be explained by the theory of Shattuck, who held that a surplus spermatozoön remained about the segmenting morula and was held between its component cells to later fertilize a primordial ovum. Meckel's view that embryoma represent the inclusion of one fertilized ovum within another is also discarded.

There are objections to both of the prevailing theories. Opitz and Menge state that it is unreasonable to believe that they arise from unfertilized ova, since they may occur in parts of the body far distant from the ovary, may occur in men, and even in the testis. They state, moreover, that they would be found more frequently in the tube, since unfertilized eggs pass through that structure in tremendous number, yet only 5 authentic cases in that location have been reported. On the contrary, Pfannenstiël supports the view, arguing that the neoplasm develops from a totipotent cell and rarely occurs before puberty and practically never after the menopause.

The theory that they arise from blastomeres is receiving much support. Marchand and Bonnet are recent advocates. The theory holds that the earliest segmentation divides the ovum into two kinds of blastomeres, one type of which become germ cells and the other, somatic cells which enter into the construction of the body. The blastomeres, therefore, are the products of the first-cell division of the impregnated egg. In the complicated process of growth in the early embryonal period, some of these cells may be displaced in various parts of the developing organism. Somatic blastomeres included in the ovary might be destroyed undeveloped or, after a long latent period, might assume sudden growth and create a dermoid or teratoma. From such cells all three germinal layers may arise. Against this theory it is urged that it does not seem reasonable that these cells would be displaced chiefly in the ovary, from which organ develop the great majority of tumors. The fact that many dermoids may be noted in one ovary also argues against the theory that the embryoma arise from isolated blastomeres. As many as eleven dermoids have been noted in one ovary, and twenty in both. It seems almost impossible to believe that they all could be explained on this ground. No theory, in consequence, is without objection.

Cystic Dermoids.—Cystic dermoids are more properly known as teratomatous cysts. They differ from dermoid cysts in other parts of the body in that they contain all three germinal layers while true dermoids contain only ectodermal structures. The tumors are cystic and contain products of the skin glands which, while fluid at the body temperature, are thick and doughy when cooled. The growths consist of two parts: (1) an embryonal rudiment in which can be demonstrated tissues derived from all three layers of the blastoderm; and (2) the cyst into which the rudiment is growing.

Frequency.—The frequency is variously stated. Spencer Wells reported 2.2 per cent in his series of 1,000 ovarian tumors, yet his cases were seen only when ovarian tumors were considered operative, and dermoids rarely attained great size. Olshausen found a frequency of 4 per cent in 2,275 ovarian tumors. Later authors found higher percentages. Dermoids formed 18.8 per cent of 138 of Howard Kelly's ovarian tumors, and 18.7 per cent of 64 cases reported by Sänger. There were 98 dermoids in 1,000 ovarian tumors removed by the Mayos during 1905-1912.

Age.—Dermoids have been observed at all ages from fetal life to extreme old age. They are very uncommon except during sexual activity. More occur between thirty and forty years than any other decade. They form the majority of ovarian tumors in childhood and about the period of puberty, yet they are, nevertheless, rare at that time. Tumors which are first seen after the menopause are apt to show malignant degeneration.

Appearance and Form.—They form smooth growths, of spherical shape, except when they co-exist with cystadenomata when their form is irregular. They vary in size from a cherry seed to that of a man's head. The majority seldom exceed 6 or 7 centimeters in diameter. A few large tumors have been reported. Keith, in 1895, reported one weighing one hundred pounds, associated with a small dermoid on the opposite side. Byford, in 1898, described one weighing seventy pounds which he removed from a patient of fifty-two years who had first noticed enlargement of the abdomen twenty-five years previously.

Dermoids are usually unilateral but may affect both ovaries. Mantel, in reviewing 191 cases, found 26 that were bilateral. Gebhard, in 107 cases, found 16 bilateral. There were 14 bilateral dermoids in the Mayos' 98 cases. Manton, who reviewed the literature for a ten-year period a few years ago, found 330 dermoids reported during that time. Forty-six were bilateral. Hines found that only 309 bilateral dermoids of the ovary had been reported in the literature for the past one hundred years; of these, 90 were collected by himself, not having been included in the 219 cases compiled by others.

Dermoids usually possess a long pedicle which permits them to rise into the abdominal cavity at a fairly early period. Intraliga-

mentous development is rare (6 per cent of cases according to Lippert). Very occasionally, ovarian dermoids may be retroperitoneal. Bardenheuer and Zweifel have described dermoids in the loins which they thought developed from rests left in the descent of the ovaries. Dermoids in these unusual situations must be distinguished from dermoids of the pelvic connective tissue described by Sanger. The presence of ovarian substance is conclusive.

The tumors may replace the whole ovary, although ovarian tissue usually remains as a nodular thickening of the wall. The presence of corpora lutea shows that this tissue is functioning. Therefore, sterility is not a necessary result even in bilateral tumors. Manton recently collected 19 cases of pregnancy associated with bilateral dermoids. Dermoids may arise from accessory ovaries, as is shown by the fact that the normal ovaries are unaltered. The tumor occasionally projects from an apparently normal ovary, suspended from it by a definite pedicle. In case the pedicle becomes severed, either from torsion or the pull of adhesions, the tumor may attach itself to the omentum or mesentery.

The cysts are usually unilocular. Their contents vary. Their character is profoundly affected by torsion of the pedicle. Both the dermoids and solid teratoma are frequently seen with ovarian cystoma; Arnspenger noted the association in 14 per cent of cases. They are most often found with the pseudomucinous type when they are likely to break through the septa and occupy the center of the tumor. They may occur with simple serous cysts, papillary growths and corpus luteum cysts.

Structure.—In contrast with the true dermoids of other portions of the body, ovarian dermoids are rarely lined with skin. This structure is confined to the embryonal rudiment, or to its immediate neighborhood. The peripheral cyst wall which does not belong to the actual dermoid anlage consists of several parallel layers of connective tissue usually loose in structure. The inner layer is rich in vessels. The remains of the ovarian substance lie in the outer layer. The inner surface of the cyst is at first covered with a low stratified or cubical epithelium, occasionally suggesting amnion. Later, this epithelium is destroyed, because of irritation by the hair and by the secretion from the skin glands of the embryoma and is replaced by reddish brown layers of granulation tissue containing numerous giant cells where the hair shafts cut in, and with infiltration from hemorrhage. Areas of calcification may be seen in the older and larger tumors.

A rounded mass is usually found projecting from the wall into the cyst cavity. This is the dermoid plug which contains in varying proportions structures derived from all three embryonic layers, usually with a marked preponderance of ectoderm and especially of the structures of the cephalic end of the body. Wilms considers it a rudimen-

tary embryonal formation which is hindered in its development by the confined space of the cyst cavity. Because of mechanical disturbances, only the tissues which are first differentiated in the embryo come to full development. Thus, ectodermal and cephalic structures are more abundant than those derived from the entoderm.

The embryoma tends to follow in a rudimentary and distorted manner the arrangement of the fetal structures. The thick skin and abundant hair represents the scalp. Under this are plates of bone representing the cranium. A firm connective tissue corresponds to the dura, under which are representatives of brain tissue. There are also other portions of skull tissues—jawbones, teeth, and epithelial organs of the buccal cavity. The respiratory and intestinal tracts are least developed. They may present only as tubes lined with cylindrical or ciliated epithelium.

Occasionally, the dermoid plug does not project into the cyst lumen. It is indicated by a thickened area in which are bunches of hair lying flat on the cyst wall. On section, however, one may demonstrate typical fetal structure.

Few structures of the body have not been represented in dermoid cysts. The skin contains sebaceous and sudoriferous glands. Even the erector muscles of the hair have been described. Hair is constantly present and the strands may be as long as a meter. The color is usually reddish brown, although it may be anything from white to black. The color may not resemble that of the patient and may vary in the same cyst, and even in the same strand. Sometimes the hair pierces the opposite wall of the cyst and grows through it when the process is attended by a giant cell reaction.

Wilms states that there are always tissues of the central nervous system, even in dermoids the size of a pea. Occasionally, the structure may be differentiated in a most remarkable manner, yet this occurs only in the larger tumors. Rudiments of eyes are common. They may be accompanied with eyelids and lashes. Rudimentary ears have also been found. The peripheral nervous system is not as well developed as the central, although there may be large nerve trunks and even suggestions of the gasserian ganglion. Sympathetic ganglia have also been described within the muscle wall of the intestinal tract. The cranial bones may be remarkably developed. Teeth are extremely common and may be well developed, although they usually present as rudiments. Sometimes large numbers of teeth are found; Schnabel reported one hundred and Ploquet three hundred in a single dermoid. Mammary glands have been described by Sutton, Reverdin, and von Velits. There was colostrum in the case of the latter.

Derivatives of the mesoderm may be represented nearly as well as those of the ectoderm. The arrangement tends to approach the normal. Smooth muscle occurs commonly, striated muscle quite

rarely. Cartilage is common. Askanazy claims that fibrocartilage is as common as hyaline. The bones may even contain marrow. Blood vessels may attain remarkable development. In one of Wilms' cases, a large artery sent branches to the buccal cavity and to the brain (internal and external carotid). There may even be blood constituents in the lymph follicles and bone marrow.

Entodermic structures are much less developed. They appear usually in most rudimentary form. Thyroid tissue lies by the side of the trachea. It may even be recognized macroscopically. A larynx and vocal cords have been reported by Kroemer. Other parts of the respiratory tract, as atrophic lung rudiments containing bronchi opening into a rudimentary trachea, have been described by Wilms. The respiratory part of the nose with a nasal septum has also been noted. The intestinal tract may be represented by canals with typical epithelium, intestinal villi, and glands, smooth musculature, solitary lymph follicles, and Peyer's patches. There may be embryonic stomachs, small and large intestines. Loops of intestine with a mesentery rarely attain size to be recognized macroscopically. Pommer has reported a cecum with an appendix.

Rudiments of the liver, kidney, and pancreas have not been demonstrated. Von Recklinghausen found a structure resembling the wolfian body. Kroemer described what appeared as müllerian tissue consisting of an endometrium lying on a thick layer of smooth muscle with cervical stroma and epithelium and vaginal mucosa.

While these tissues commonly present as isolated remnants, there is, in rare cases, more complete development of the embryo. This occurs in tumors the size of a head or larger and, according to Wilms, only when there is not much cyst pressure. Nearly the entire fetal body may be recognized macroscopically. Axel Key described a fetus attached by the head, having a bony skull, brain, jaws, and two lower extremities with toes. There was hair on the scalp and on the mons veneris. Repin found a complete skeleton, on the right side of which was a complete bony framework, even including phalanges. Askanazy's case was a misformed fetus with a head, having two hair bundles, a brain, a pigmented eye spot, an ear and body with two legs with toes, and a pubic region presenting a rudimentary clitoris and corpora cavernosa. Shattuck found an acardiacus with lower extremities, vulva, pubis, perineum, pelvis, vertebra, and a blind intestinal loop.

No sign of fetal membranes has ever been described.

Atypical Forms of Dermoids.—These are also called biphilloma. They contain only ectodermal and mesodermal derivatives. Kroemer says they constitute 5 per cent of all ovarian dermoids. Cases have been described by Wilms, Kroemer, Neck, and Namvenck, Askanazy and others. The diagnosis can be made only by serial sections, since

it depends upon absence of the entodermic layer. The case of Saxen, which presented a single tooth in an otherwise normal ovary, is the extreme type of this condition. Some, as Hanan, Ribbert, Landau, and Pick have advanced the theory that there may be suppression of the ectoderm and overgrowth of the entoderm in atypical dermoids. Some would see pseudomucinous cystadenoma as the expression of a one-sided development of the intestinal part of a teratoma, a theory which has not met the approval of others.

Multiple Dermoids.—Multiple dermoids are not unusual. Novak, in 1909, was able to collect but 21 cases from the literature: 7 of these were bilateral. He added 2 cases. One case, a woman of thirty-nine,⁴ had ten dermoids in the right ovary and eleven in the left. Some embryonal rudiments had a very complicated structure. He found skin, hair, sebaceous and sweat glands, central nervous system, ganglia, peripheral nerves, meninges with chromatophores, corpora amylacea, buccal cavity with salivary glands and teeth, pharynx with tonsil, intestinal mucosa, thyroid, cartilage, bone and smooth muscle. There was also tissue which was either a prostate or adenomyoma and, what was never before described, a structure resembling a hypernephroma. Other dermoid plugs showed a very simple structure. The other case was a seventeen-year-old girl containing six dermoids in the right ovary and four in the left, completely separated from each other. Some showed highly differentiated structure. The largest number of multiple dermoids reported before Novak's case was that of Schroeder in which there were four dermoids in one ovary and seven in the other. Wilms states that there must be a complete fetal rudiment in each anlage for true multiplicity, since the condition may be simulated by transplantation of elements, especially when the dermoid constitutes one part of a large cystadenoma. The secondary cysts in these cases do not show the typical embryonal rudiment.

Malignant Degeneration of Dermoids.—The cystic teratomata are, in general, benign tumors. They grow slowly, remain inclosed in a definite capsule, and do not possess invasive properties. Rupture of the cyst and dissemination of its contents may be followed by implantations upon the peritoneum, although this is not the rule. When it does occur, there result tiny cysts with typical dermoid contents, some with, and some without, hair. An inflammatory reaction usually incloses the escaped tumor contents. An independent growth of these implantations, such as occurs in pseudomyxoma peritonei, has not been reported.

CARCINOMATOUS CHANGES.—Carcinoma may develop in an ovarian dermoid in three ways: (1) by direct extension from a carcinoma of an adjacent organ, or by metastases from a more distant one; (2) by extensions from a carcinoma which has developed in the ovarian tissue not concerned with the dermoid growth; the carcinoma of the ovary may be

primary, as in malignant degeneration of a preëxisting cystadenoma, or metastatic, from primary cancer elsewhere; (3) by malignant degeneration of the epithelial structures of the dermoid itself.

Carcinoma arising in the epithelial structures of the dermoid itself is considered a rather rare condition. Yet Spalding believes that more cases will be found if all dermoids are subjected to careful, gross and microscopic examinations, since the tumor is constantly exposed to chronic irritation by the hair and other cyst contents.

Lippert estimates the frequency of carcinoma arising within the dermoid as 3 per cent. Yet Williamson and Barris, in 1911, could collect only 32 cases which had been reported in the literature. Furthermore, a critical analysis of the reports convinced them that the evidence was not sufficient in 14 cases to warrant the diagnosis that the cancer had originated in the dermoid tissue. Frankl, in 1920, states that he was able to collect 60 cases when adding a case of his own. Since then, cases have been reported by Spalding, Boettger and Eisenstadter. Practically all of the cases are squamous cell carcinoma. They are usually of the cornifying type arising from the dermoid skin. There are only two cases reported of glandular carcinoma. Friedlander's case was an adenoma of a sweat gland. Yamagiwa's case was supposed to arise from an anomalous mammary gland. Although carefully described, there has been objection to the diagnosis.

Squamous epithelial cancers are more common because of the greater activity of the epiblastic elements of the tumor (Boettger). Frankl suggests that the carcinoma may be of the same age as the dermoid and may arise from the first cells, a point which is only theoretical. The majority feel that the cancer arises from the cells of the differentiated tumor, either in the dermoid plug, or in the wall of the tumor.

The results of operation have been usually bad, since the case is most often well developed when it comes to operation. Spalding calls attention to the fact that the prognosis of early cancers should be very good because of the thick, protecting capsule of the dermoid. Yet there are few cases which have been presented as convincing cures. Williamson and Barris' case lived seven years after her operation at sixty. Pfannenstiel's case remained well eight years after operation, as did Boestrom's for eleven and a half years after operation.

SARCOMATOUS DEGENERATION.—Sarcomatous degeneration of a dermoid occurs far more rarely, since it is more apt to be noted in association with a dermoid, when it arises from the ovarian tissue not included in the dermoid. Two cases of melanosarcoma arising in the dermoid skin have been described by Amann and Lorraine. The tumor pigment was identical with the color of the hair in both cases. Ludwig described two nonpigmented sarcoma. Holtschmidt's case occurred in a cyst whose buccal cavity contained teeth. Schwertassek described 6 cases of round- or spindle-cell sarcoma. Kroemer found 1 case which may be of endothelial origin.

COMPLICATIONS OF DERMIDS.—Complications are rather common,

especially torsion of the pedicle. Sanger found 6 cases of torsion in 33 dermoids. Storer, in 248 cysts, which had undergone torsion found 43 dermoids (17.5 per cent). Infection was formerly common after torsion. It resulted from operative interference, the trauma of labor, or by extension of infection from neighboring organs. Even when sterile, the



FIG. 74.—DERMOID CYST OF OVARY WHICH HAD OFFERED OBSTRUCTION TO LABOR. The masses of light-colored hair are clearly shown.

cyst contents are extremely irritating to the peritoneum. Rupture of a cyst may be followed by chemical peritonitis.

Dermoids often complicate pregnancy. They do not appear to favor sterility, since Manton, in 331 cases, found 73 single and 19 double dermoids associated with pregnancy. Ehrenfest removed a dermoid cyst of

one ovary about the fourth month of a first pregnancy. He left at the time a small dermoid on the other ovary. The pregnancy terminated normally and the patient has since borne another child. The dermoid is likely to prolapse in the pelvis and fall in advance of the fetal head. We have seen 2 such cases.

SYMPTOMS.—There is nothing characteristic in the symptoms. They may be slight, or absent. Menstrual disturbances are very uncommon. The patient may complain of a feeling of weight in the pelvis or a sense of pressure on the bladder and rectum. The various complications carry their own symptomatology.

DIAGNOSIS.—The position of the tumor often gives a hint as to the diagnosis, since the long pedicle permits the growth to rise early in the abdomen. Large amounts of characteristic contents, as hair, may be recognized by the examining fingers. Occasionally, a bone may be felt. The X-ray may give valuable information. The diagnosis may be more difficult when dermoids are present with other tumors, as fibroids and pseudomucinous cysts. The fact that they occur frequently in infantism or genital malformations should excite the suspicion that the tumor is a dermoid.

TREATMENT.—The treatment is operative removal, without puncture of the cyst, after careful inspection of the other ovary. The tumor should be examined immediately for evidence of malignant degeneration.

PROGNOSIS.—The tumors are benign and remain cured after operation, unless there has been malignant degeneration. The prognosis, therefore, is governed by the presence or absence of complications.

Teratoma.—The solid teratoma are much more rare than the cystic teratoma or dermoids of the ovary. They resemble them in that they usually are made up of all three germinal layers. The tissues, however, are of the early embryonal stage, and do not reproduce the highly developed and differentiated body structures which may be presented in the dermoid tumors. On the contrary, the cells usually occur in a confused and complex mass described by von Rindfleisch as a histological potpourri.

Robert Frank, in 1907, was able to collect but 52 certain cases from the literature. He found 4 other doubtful ones. It is a disease of youth and middle age. Rowland Harris, in 1917, found 21 cases in patients under fourteen, 9 of which had been included in Frank's statistics. The 2 youngest cases were three years, and three years and eight months respectively. The oldest of Eden and Lockyer's 16 cases was thirty years. Frank found 4 still older, the oldest of which was forty. No case yet described was present in a woman who had reached the menopause. Twenty-two of the patients in Frank's series had never borne children. Nine had been pregnant. No details are given in the remainder of the cases.

The teratoma, almost without exception, are unilateral, well-pedunculated tumors, which rarely present adhesions except as a con-

sequence of torsion of the pedicle. They form coarsely nodular tumors with rounded contour. They may preserve the form of the ovary. The size varies. The small tumors are found usually only accidentally, or when there are complications as torsion of the pedicle. The growth may attain considerable size. Falk's case weighed fifty pounds at post mortem.

The rate of growth is extremely rapid in cases which have been under observation. The tumor was known to be present for seven and a half months before operation in 24 of Frank's 52 cases.

On section, the tumors are never entirely solid, since they contain cystic spaces of various size lined by epithelium. Some may resemble solid carcinoma from which they may be distinguished only with a microscope. Usually, however, the sebaceous content of the cysts and the presence of hair indicate their nature. Not all cysts present these structures. Some have a smooth mucous lining, and a clear mucous content. Inspection of the cut surface of the tumor often shows islands of bone and cartilage, or the rudiments of teeth. The section may be mottled with punctate points of black pigment, or discoloration due to hemorrhage.

Microscopic section shows a coating of fibrous tissue. In this may be ovarian stroma. Functionating tissue is more likely to lie near the pedicle. The groundwork of the tumor is composed of embryonic tissue in which is scattered the various epithelial structures. The embryonic connective tissue may appear as if myxomatous or sarcomatous. The entire mass is divided into lobules by thin connective tissue septa.

The ectodermal structures are variously represented. Some tumors contain only skin-lined cysts, without other epidermal structures. Others present skin containing hair, sebaceous and sweat glands. There may also be rudiments of young teeth. The brain is represented by islands of rudimentary nerve tissues. The ventricle is suggested by irregular tubules and may be identified by the high embryonic neuro-epithelium. A choroidal plexus may be very well marked. There may be primitive eyes which often contain pigment of the retina or choroid. Neuro-epithelioma and glioma have been observed arising from the brain structures. Adenocarcinoma has been described arising from glandular tissue.

The mesodermic structures are well represented. There may be elastic or fibrocartilage, or hyaline cartilage. The latter is more common and may be surrounded by perichondrium. Bone may be present as partly calcified spines with well-developed osteoblastic areas. Smooth muscle may occur in large quantities and, contrary to the condition found in dermoids, the striated muscle may be well developed.

The entoderm is represented by the high, columnar epithelium of the intestinal tract. Occasionally, it is differentiated into recognizable

or intestinal rudiments. There may be ciliated epithelial canals of the respiratory tract, accompanied by mucous glands, hyaline cartilage and smooth muscle.

The tumors metastasize usually by peritoneal implantation, although there may be direct extensions to the retroperitoneal lymph glands. A few cases have shown visceral metastases in the liver, lungs, or brain. The metastases are usually of indifferent embryonic sarcomatous tissue, yet complex teratomatous metastases have been observed in the peritoneum, in the retroperitoneal glands, and in the liver.

Struma Ovarii.—This is a tumor of the ovary which is composed largely or wholly of tissues more or less closely resembling normal thyroid. The structures contain iodine. They are usually malignant, give metastases, and produce ascites. They represent teratoma in which one germinal layer has developed far in advance of the others.

Pick is responsible for creating interest in this most unusual tumor. He called attention to the fact that the tumor described by Gottschalk as folliculoma malignum strongly resembled adenoma of the thyroid. Since he found thyroid tissue in six of twenty-one teratoma, he argued that thyroid tissue might so overgrow the remaining structures of a teratoma that it would remain as the only recognizable element. Saxen's case of a single tooth in an otherwise normal ovary appeared to substantiate this view. Others, as Kretschman, believed that they were metastases from primary thyroid tumors. Walthard's work confirmed Pick's view. He proved the teratomatous elements in three so-called thyroid tumors by serial sections. Such work was necessary, since stratified squamous epithelium, sebaceous and sweat glands were found only in nine successive sections of an ovarian tumor which appeared to be constituted entirely of thyroid tissue. The presence of iodine in the alveoli was demonstrated by Robert Meyer, thus disproving the view of those who regarded the growth as degenerations of ordinary cystadenoma.

Trapl made the interesting observation that, after removing the ovarian thyroid, there was compensatory hypertrophy of the normal thyroid, suggesting that the tumor gave off an internal secretion. Trapl studied the frequency of other teratomatous tissues in the so-called thyroid tumors. The thyroid structure was present alone in 5 cases. There were bone and cartilage also in one, bone and muscle in one, cartilage and sweat glands in one, a ductus thyroglossus in one, structureless connective tissue in one, cartilage and squamous epithelium in one, squamous epithelium and sweat glands in one, hair, skin and intestinal rudiments in one, bones and two teeth in one, and epidermis and hair in one other. These observations were necessary to place the teratomatous structure of the tumor on a firm basis, since Bauer has recently described a similar tumor which seemed to arise by down-growth from the superficial ovarian epithelium.

It appears as if struma ovarii may occur in two forms and be either

benign or malignant. Errors may readily arise from difficulty in interpreting the histologic picture of the tumor. Thus, the normal fetal thyroid before the appearance of the alveoli is composed of compact cell masses which may erroneously suggest carcinoma. Malignancy is the rule, however, in the thyroid ovarian tumors. Kretschman's case died from recurrence two and three-fourth years after operation. The cases of Polano, Katsurada, Glockner, Gottschalk, and Walthard were considered malignant, and reported as clinically cured. The case of Vagedes has borne a child since her operation.

MESODERMAL DEVELOPMENT OF A TERATOMA.—The question of whether there may be one-sided mesodermal development of the teratoma has not yet been definitely settled. The cases of Reiss and Jung of ovarian enchondromata have been so considered by a number of authors. The fact that Reiss' enchondromata recurred as a carcinoma caused Pfannenstiel to believe that it should be classified as true teratoma.

SYMPTOMS OF TERATOMA.—Pain is usually an early symptom. Intestinal disturbances are generally noted. There may be diarrhea, or constipation, often due to pressure or a reflex phenomenon following torsion. Vomiting, nausea and anorexia accompany torsion of the pedicle. The abdomen may rapidly enlarge from growth of the tumor mass or the development of ascites. The latter is present in more than half the cases. An unusual feature in Harris's case was precocious sexual development, since menstruation took place in a child of five, seven months before removal of the tumor. The phenomenon disappeared after operation. This symptom has not occurred in other cases in which the tumor appeared before puberty.

DIAGNOSIS.—The diagnosis, in view of the very great rarity of the tumor, can seldom be made before operation. The diagnosis of malignancy can ordinarily be made at operation. The exact nature of the growth is usually determined when the tumor is sectioned after removal.

TREATMENT.—The treatment is operative removal. Because the tumors are ordinarily malignant, the operation should consist in removal of the adnexa of the affected side as widely as possible, and supravaginal hysterectomy together with the adnexa of the opposite side.

PROGNOSIS.—The prognosis is not good. The outcome was not known in 10 of the 37 cases collected by Frank. Two cases were alive and well for short intervals, namely, one and six months after operation. There were only 3 other cases living, 2 presenting recurrences. One was well after eight and a half years.

Pfannenstiel's series is a little more encouraging, yet since it was collected about the same time as Frank's, it is not possible to say how far the series overlapped. Of 42 cases, the outcome was not known in 6; 4 unoperated cases died. There were 5 deaths, or 16 per cent, in 32 operations. Of the 27 survivors, 16 died from recurrence within one and a half years (59 per cent). Four were lost after a short period of observation. Of the

remaining 7, 1 was well one and a half years, 1 at four years, 1 at five years, 1 died at six years from tuberculosis without evidence of recurrence, 1 was well at eight years, 1 at eight and a half years, and 1 at ten years. Thus there were 4 cases of the 32 which remained cured for five years.

STROMATOGENOUS TUMORS

The stromatogenous ovarian tumors are of the connective tissue type and develop from the ovarian stroma. They are neither as common, nor of as great clinical importance, as the epithelial neoplasms. They are divided into three general groups: (1) benign tumors of the connective tissue type; (2) sarcoma; and (3) periendthelioma and endthelioma.

Under the benign stromatogenous ovarian tumors are grouped fibroma, myoma, osteoma, chondroma, hemangioma, and lymphangioma.

Fibroma and Myoma.—Ovarian fibromyoma and myoma are rare tumors. Together they constitute about 2.5 per cent of all ovarian tumors. There are comparatively few series of size. Basso has reported 4 cases and has collected 45 others from the literature. Kroemer found only 5 in 280 ovarian tumors. Löhlein found 7 in 172 ovarian neoplasms, of which 2 were bilateral. Kroemer studied 19 cases of which 17 were fibromyomata and 2 pure myomata. Peterson has collected 84 cases of fibromyomata.

Little is known concerning the etiology. It is rather remarkable that these tumors occur so rarely, since scar tissue theoretically results in the ovary as a monthly phenomenon during menstrual life. It is prevented from developing by the unique method by which the corpus luteum is absorbed.

The age at which fibroids have been found ranges from eight to eighty-three years. They are rarely observed before the age of twenty-five and are found most frequently in the fourth and fifth decades.

These tumors are probably most frequently derived from the tissues of the ligamentous supports of the ovary rather than from the ovarian stroma. They are usually unilateral and are bilateral only in about one-fifth of the cases. The bilateral cases are often associated with uterine fibroids which they resemble in nearly every way. They grow slowly but may attain considerable size. Whitridge Williams' patient carried her tumor for thirty-seven years; it weighed twenty-two pounds. The largest tumor of which we find record is Clemens, which weighed forty kilograms, and whose presence was known for ten years. Spiegelberg and Jacoby both described tumors weighing thirty kilograms. Stürmer reported a tumor that weighed seventeen and a half kilograms in a Hindu woman.

The ovarian fibromata may present as diffuse, or circumscribed, growths. In the former, the whole ovary is replaced by the new growth, while the latter is localized to one part of the ovary or arises from that organ by a definite pedicle.

The diffuse fibroma usually retains the normal contour of the ovary until it has attained considerable size when it presents a spherical or ovoid contour. Infrequently, it is of kidney shape, with a marked indentation at the hilus. The circumscribed forms are often found in a lateral pole of the ovary. They are not encapsulated and there may be no sharp line of demarcation between the normal tissue and the neoplasm. Normal stroma may always be found on their outer surfaces. These tumors are well-pedunculated, firm, hard growths. On gross section, they appear of white or grayish white color. The cut surfaces are sometimes mottled by hemorrhage. The characteristic whorl-like arrangement of fibrous tissue is invariably present. Under the microscope the tumors present the characteristic appearance of fibroids in general. There are varying proportions of connective tissue cells and fibers and blood vessels. The younger and smaller tumors are the more cellular. The tumor fibers are often arranged concentrically about the blood vessels which are usually merely capillary spaces lined by epithelium. The tumor may contain soft areas because of edema or myxomatous degeneration. Cystic spaces may result from degeneration or from lymphangiectasis. Calcareous degeneration is not often found. Rarely, necrotic areas may be more or less encapsulated within a calcified shell. Occasionally, a corpus fibrosum or corpus luteum is filled with calcareous deposits when it becomes a so-called "ovarian stone."

Rokitansky called attention to a fibroma which arose from a pathological increase in the connective tissue of a corpus fibrosum. The "ovarium gyratum" of Adler is due to a superficial fibrosis in the cortex of both ovaries which replaces that layer and causes an enlargement of the ovary. This hypertrophy is subsequently followed by atrophy and the ovary presently becomes extremely firm, with a markedly corrugated cortex. Very often, one finds small, superficial, papillary fibromata appearing on the side of the ovary rather near the hilum. They are wartlike structures which are of no clinical or pathological significance, except for the fact that tumors of more serious import are sometimes mistaken for them. Early superficial papillae of solid cystadenomata and some of the implantation metastases from malignant tumors may resemble them in a rather general manner. They are usually more crenated, however.

Symptoms.—The clinical symptoms vary and are usually slight until the tumor attains considerable size. There is no definite relationship between the tumor and menstrual disturbances unless the growth is bilateral, when it may be accompanied by amenorrhea and

sterility. Peterson believes that the menopause is usually retarded in single tumors. Dysuria is a rather common complaint. The majority of the symptoms are caused by the size of the tumor or by complications. They are very likely to follow adhesions which were noted by Peterson in 36 per cent of 84 collected cases. Ascites is common, especially in tumors of appreciable size. It occurred in 40 per cent of Peterson's series. Some claim that it regularly accompanies the diffuse fibroids but is uncommon with the circumscribed forms. There may be large amounts of the ascitic fluid. Olshausen found twenty-two and a half liters in one of his cases. Ovarian fibroids are rather frequently associated with other genital malformations. The bilateral tumors often coexist with uterine fibroids. The tumors may block labor when they have prolapsed during pregnancy into the pelvis and are in advance of the fetal head. Cachexia is common with the large tumors.

Diagnosis.—They cannot always be differentiated from other solid tumors of the ovary, especially since they often present certain features usually associated with malignancy, namely, ascites and cachexia. The history of slow growth is of value when it is possible to obtain it. The tumors are often mistaken for a malignant condition in the liver associated with ascites. One of us has seen 2 cases which were considered inoperable cancer and had been treated only by tapping. Both recovered after operation.

Prognosis.—The prognosis is good, since the tumors are benign.

Treatment.—The treatment is operative removal. This usually may be done without difficulty, since the tumors are usually well pedunculated and the adhesions are not extremely dense.

Osteoma and Chondroma.—The majority of the tumors described as osteoma are really fibroids which have undergone calcification, the deposit consisting of a structureless mass of lime salts. True bone formation with periosteum and marrow has been described only in connection with the dermoids and teratoma.

There is considerable discussion as to whether there may be a true chondroma of the ovary. Most of the tumors described as such are now considered atypical teratoma. Jung reported a case which he believed was due to a metaplasia of the ovarian stroma. Kroemer, and some others, agreed with the diagnosis, yet Robert Meyer regarded it as a mesodermal teratoma and Kehrer thought it was a mixed tumor from mesodermal rests of the müllerian duct.

Myxoma.—True myxoma of the ovary has not yet been described, although myxomatous degeneration is often seen in fibroid tumors. Myxosarcoma will be considered with the sarcoma (page 373).

Angioma.—True hemangioma of the ovary is exceedingly rare. It is often confused with tumors presenting a marked dilatation of the venous system, a condition which may occur in ovarian tumors with

extreme and longstanding passive congestion. Marckwald reported a hemangioma the size of a hazlenut in the median pole of an ovary in which was beginning a papillary cyst. Kroemer reported a small one found in a serous cystadenoma. Bilateral ovarian hemangiomata have been described by Orth, and Payne. Orth's case was a child who also presented similar tumors in the skin and in several of the inner organs.

Lymphangiomata may present as tumors distinguishable from lymphangiectases which are often seen in ovarian fibroids. They are grayish white tumors which bear some resemblance to fibromata, although they are not so firm. On section, they present a meshwork of cystic cavities, varying in size from a pinhead to seven or eight centimeters in diameter. The cysts are lined by a delicate endothelium, and contain a slightly turbid light-colored fluid. There is no epithelial débris. There are few blood vessels in the tumor. Kroemer has reported 2 cases, one of which showed considerable proliferation of both the endothelium and the stroma.

Sarcoma of the Ovary.—Sarcoma of the ovary is a rare tumor. It may be a primary growth, may represent a malignant degeneration of an ovarian fibroid, or may occur as metastases from tumors primary elsewhere in the body.

Little is known concerning the etiology. They have been observed at all ages from fetal life to women of the sixty-sixth year. Forty per cent of reported cases have been observed in women less than twenty-five years of age. The average age of incidence is thirty-two years. Hubert collected 200 ovarian sarcomata in children, 6 of which occurred in the fetus.

PRIMARY OVARIAN SARCOMA.—Primary ovarian sarcoma is a malignant neoplasm of mesodermic origin. There are several histologic types which may present singly or in combination. Thus, there are spindle-cell, round-cell or mixed-cell sarcoma. Myosarcoma, chondrosarcoma, and melanosarcoma have also been described, yet there is much doubt as to whether these are other than sarcomatous changes in dermoids. Myxosarcoma is rather common.

In their gross characteristics, they rather resemble ovarian fibroids. They are solid tumors with a smooth or slightly nodular surface, which tend to preserve the general shape of the ovary, although they may be rounded or oval in form. They are nearly always pedunculated and are not nearly as likely to be bilateral as are the ovarian carcinoma. Bilateral growths occur in rather less than one-third of the cases. The round-cell type are more frequently bilateral than the other ovarian sarcoma.

The sarcoma grows rapidly. The cellular types show the most rapid development. Tumors occurring in young patients, and especially those which develop during pregnancy, may attain very large size within a comparatively short time. Chrobak reported a round-cell

sarcoma which, in twenty-three days, increased from the level of the umbilicus to the margin of the ribs.

On section, they are firm and resemble the fibroids, especially the fibrosarcomata. The round-cell types exhibit a softer and more friable surface. They are white or pinkish in color. Older tumors may present a yellowish tinge. Degenerative changes are common and include fatty degeneration, necrosis, hemorrhage into the tumor substance, and thrombosis. Cysts may result from softening or from lymphangiectasis.

Under the microscope, the fibrosarcomata appear very cellular. The spindle cells are closely packed but irregularly distributed. They may appear to form the walls of new blood vessels which are present in great abundance. The cells vary greatly in size and shape and in the chromatin content of their nuclei. Mitotic figures are common. Myxomatous degeneration frequently occurs in older tumors. Some of the sarcoma contain many large irregular cystic spaces lined by a ragged layer of sarcomatous tissue and containing serous or bloodstained fluid. They may result from dilatation of the lymph vessels or from liquefaction necrosis.

The cells of the round-celled sarcoma are somewhat more uniform in size. They are small and round, with relatively large, deep staining nuclei, surrounded by clear protoplasm. They also may be arranged diffusely and tend to be grouped about newly formed blood vessels. Sometimes they show an alveolar arrangement when the individual cells are separated by a delicate connective tissue stroma. Tumors of this group also have a strong tendency to necrosis, softening, and hemorrhagic infarction.

Tumors of the mixed-cell type are also found containing not only round and spindle cells but multinucleated giant cells as well.

Myosarcoma.—Myosarcoma has been described by Kroemer. It consists of round and spindle cells, together with a considerable proportion of smooth muscle fibers, some of which showed a marked hypertrophy.

True chondro-osteosarcoma have not been described. A number of cases regarded as such are now placed in the teratomatous or mixed tumor grouping.

Myxosarcoma.—Tumors consisting entirely of myxosarcomatous tissue have never been described. However, myxomatous areas are frequently seen in all types of sarcoma of the ovary.

Melanosarcoma.—Melanosarcomata are occasionally found. In the majority of cases, they probably represent metastases. They are found most often when there is a general melanosarcomatosis, the primary tumor usually being in a cutaneous nevus. Frankl has collected 40 such cases. Very rarely these tumors appear to be primary in the ovary. Loubergran and Rives collected 7 such cases. Herzog reported

another and added 2 more to the list, those of Cotton and Markus. Herzog, however, calls attention to the fact that the larger proportion of cases reported as primary are really not such but are rather secondary, to some small skin nevus, which was overlooked. The only 2 cases which he believes are undoubtedly primary are those of Amann and Lorraine. These did not arise directly from ovarian stroma but sprang from pigment cells in an ovarian dermoid. He calls attention to the fact that secondary melanosarcoma of the ovary may occur in two forms, a large homogeneous tumor which completely replaces the normal ovary, or as small disseminated nodules which are scattered through the stroma. Pregnancy appears to have been an important factor in causing dissemination of the growth in several cases.

Perithelioma, Angiosarcoma.—Although all sarcomata show a tendency to develop about blood vessels, there is a certain group in which the unit of growth appears to be the small blood vessels and the tumor seems to arise from the vessel wall. In this group from the very beginning, there is a new formation of small blood vessels, often of remarkably even size. The cell proliferation holds pace with the new formation of blood vessels. The sarcoma cells fully replace the vessel walls down to an extremely fine intima and endothelial membrane. This type of sarcoma is usually described as perithelioma. Kroemer calls attention to the fact that there is no definite perivascular lymphatic sheath or definite perithelium and feels that the term "hemangiosarcoma" better describes the condition. Lymphangiosarcoma may develop from such perivascular cells as lie about lymph vessels. The sarcoma cells form fine, netlike strands about the lymph spaces. The tumor may contain large giant cells. These tumors are frequently confused with the so-called endothelioma.

Metastatic Ovarian Sarcoma.—Secondary ovarian sarcoma is even more rare than the primary growths. They are very likely to occur in general melanosarcomatosis. The ovaries become involved by extensions through the lymphatics. The ovary may also become involved by implantation metastases through the peritoneal cavity when a uterine sarcoma has broken through the serosa, a rather rare condition. Circumscribed sarcoma nodules in an ovary which otherwise present as normal, suggest metastatic growths.

METASTASES FROM OVARIAN SARCOMA.—Sarcomata of the ovary spread by direct extension to the bowel, broad ligament, and the pouch of Douglas. The growth is soon disseminated by metastases in the order of frequency to the uterus, tubes, stomach, liver, intestines, lungs, diaphragm, kidneys, navel, vertebra and subcutaneous tissue.

The malignancy varies greatly in the different types of growths. The more cellular structures exhibit more striking features of malignancy and are more likely to involve both ovaries.

SYMPTOMS OF OVARIAN SARCOMA.—The symptoms vary considerably.

They may be lacking until the growth has attained much size. Occasionally, the presence of a tumor constitutes the only symptom. More often, there is enlargement of the abdomen due to ascites, a condition which is noted in about 70 per cent of cases. Later, there is pain, loss of weight, disturbances of digestion, cachexia, and other features of the late stages of malignant disease. Menstrual disturbances are common and may occur when the tumor is not large. There may be menorrhagia or amenorrhea, rarely metrorrhagia. When the tumor develops in early youth, there may be precocious puberty. Reappearance of the menses after the climacteric is not unusual.

TREATMENT.—The treatment is removal of the tumor, together with the adnexa of both sides and the uterus by as wide a dissection as appears feasible for the individual case.

PROGNOSIS.—The prognosis for sarcoma is not good. Cures may be obtained more commonly in the fibrosarcoma than in the other types, yet nothing but palliative relief will follow the removal of a tumor which has evidenced glandular involvement. The round-cell sarcomata are very malignant and cures average only 30 per cent in the majority of cases that have been observed as short a time as two years. There are no series of size which have been followed for five years. The literature abounds with cases in which recurrence has occurred in a few months after operation.

Endothelioma Ovarii.—There is much dispute concerning this group of tumors. The endothelial cell occupies a more or less intermediate position between the connective tissue and the epithelial cells. It is a modified mesenchymal cell, retaining its ability to behave like a connective tissue cell while, morphologically, it appears as an epithelial cell and acquires some of its functions. Tumors derived from it naturally show mixed characteristics. Thus some of the tumors resemble sarcoma while others approach the type of carcinoma. This has led certain authors, as Barrett and others, to believe that many of the tumors described as atypical carcinoma and sarcoma are really of endothelial origin. Others hold that there is not yet proof that any ovarian neoplasm has developed from the endothelium. This school is represented by Meyer and Ribbert. Certain it is that the majority of the tumors reported as endothelioma soon after the type was defined are now believed to have some other origin. Thus Schlagenhauser and Polano showed that many of them were metastatic carcinoma, while others were struma ovarii.

Leopold, in 1874, reported the first example of endothelioma, calling it lymphangioma cystomatosum. In 1879, Marchand described two ovarian tumors which he felt were derived from the endothelium of the lymph or blood vessels. They bore certain resemblances to sarcomata. Isolated cases were reported during the next decade and until Pick, in 1894, made the first detailed study. He divided them into three

morphologic types: (1) those having an alveolar arrangement; (2) those having a columnar arrangement; and (3) those having a tubular or glandular arrangement. Later study has shown that all these types may be and frequently are present in one tumor.

Barrett, in 1907, reported 85 cases which he regarded as authentic and added a case of his own. In addition to these, he cites a considerable number of cases which he has been unable to verify. He drew up the following clinical picture from a study of the cases. The age incidence was from seven to sixty-four years. The greatest number occurred in the fifth decade. Heredity did not appear to have much bearing upon etiology. The symptoms developed suddenly. Many cases were operated after the tumor or its symptoms had been observed for only a few weeks. Pain in the pelvis was a frequent complaint. There was seldom menstrual disturbances. Marasmus and cachexia were occasionally seen. The presence of the tumor formed the only complaint in a few cases.

The tumors varied in size from a walnut to a mass weighing ninety-three pounds. The majority were of the size of a child's or an adult's head. Single tumors occurred in 59 cases; bilateral in 21; not stated in 9. The remaining ovary was found to have become involved later in a number of cases. The tumors varied in consistency. Some were soft, appearing as soft as brain tissue, while others were fairly hard. Many were cystic. The rapidity of growth varied greatly. Ascites was usually present and sometimes was as much as eight or ten liters. The fluid was most often light, clear-colored, but occasionally contained sanguinopurulent material.

Metastases were common. They were found on the uterus, opposite ovary, peritoneum, omentum, liver, lungs, cord, and vagina. The mortality was very high. Thirty-one cases died a short time after operation. The majority of the 34 cases reported as recovered were followed only a few weeks after operation. Most of the cases were operated late.

Adenomyoma of the Ovary.—Not more than 8 cases of adenomyoma of the ovary have yet been described, although Norris, in reporting his case, called attention to the fact that the endometrial tissue was discovered only by microscopic examination and, therefore, might be overlooked in many cases. Microscopically, the appearance is identical with that of adenomyoma elsewhere. The older cases were thought to have developed from the mesonephros, but in the light of Webster's observations on ovarian pregnancy and Russell's and Norris's study of adenomyoma of the ovary, it seems more reasonable to believe that they have developed from müllerian inclusions in ovarian tissue. The possibility of origin from germinal epithelium has not been definitely excluded.

Mesonephric Tumors of the Ovary.—Small cysts of the hilum have occasionally been reported as having origin from remnants of the wolffian duct. Since Goodall has demonstrated that all the epithelial structures of the ovary are derived from germinal epithelium, it seems more reasonable to believe that these small tumors which present little of clinical interest are derived from germinal epithelium.

Malignant Tumors of the Corpus Luteum.—Malignant tumors composed of tissues resembling growths which have been derived from lutein cells have been occasionally reported in the literature. Some of these are thought to have developed from lutein cells. The earliest case was described by Rokitansky in 1859 and Williamson and Barris collected 9 cases.

There is, however, a group of tumors which have been thought to develop from aberrant adrenal tissue in the ovary. They are seldom found in the ovary proper but are situated in the mesovarium. They are small tumors of reddish yellow color composed of cells which resemble the structure of the cortical zone of the adrenal gland. Almartine and Maurizot, in 1912, collected 10 cases. Considerable doubt has been cast upon the possibility of an origin from adrenal rests by Glynn, who has recently reviewed all the available material. Although Aschoff and Meyer found misplaced adrenal cells in the broad ligament of 12 per cent of women studied by them, Glynn states that there is no proved case of their presence in the ovary. He states that the histologic picture of the ovarian growths which have been described as hypernephroma is quite unlike that of the large primary and usually malignant growths of the adrenal, but that it bore a much closer resemblance to the tumors usually regarded as of lutein origin. He states, moreover, that the secondary sex characteristics, precocious puberty, and other examples of suprarenal virulism are absent in these cases, although they occur extremely often in the tumors which are derived from the suprarenal cortex. On the contrary, he cites a case which he considers a true hypernephroma developing in the broad ligament. This patient showed changes in sex characteristics. Histologically, the growth was identical with that of a true suprarenal hypernephroma.

The tumors have been observed in women between the ages of thirty and sixty years. Some developed after the menopause. There is no definite relation to pregnancy. The tumors are pedunculated and often lobulated. They vary in size but may attain the dimensions of an adult head. Occasionally, they are bilateral. They may be cystic. They grow extremely rapidly and give rise to implantation growths and to general metastases. Consequently, they recur after removal. The clinical features are identical with those of other malignant ovarian tumors.

The Ovotestis Tumors.—In the rare cases of true hermaphroditism, tumors may develop from the testicular elements of an ovotestis.

There are very few cases. Pick and von Schickele both describe ovaries about the size of a mandarin orange in which, sharply demarcated from the typical ovarian tissue, were lobulated tumor masses which presented the microscopic appearance of tubular adenoma of the testis. Polano has recently described a case of true hermaphroditism in which the one ovotestis presented the typical structure of a teratomatous chorio-epithelioma.

GENERAL SYMPTOMS OF OVARIAN TUMORS

In addition to the discussion of the symptoms that we have made in individual tumors, there are certain general statements that are worthy of emphasis.

The symptoms of ovarian tumors may arise from disturbances in ovarian function, may be caused by the tumor mass, or may result from complications.

Interference with ovarian function may cause disturbances of menstruation and sterility. It is quite remarkable that menstruation so often proceeds normally in ovarian tumors of considerable size. Grouping all cases of ovarian tumors as an entity, Martin found that menstruation was normal in 75 per cent of cases. Lippert found the same condition in 43 per cent and Wedekind in 38 per cent. Moreover, it appears that various conditions, as irregularity, variations in the amount of flow, and dysmenorrhea may result solely from associated uterine disease. Amenorrhea is rather rare and is usually due to the complete destruction of ovarian tissue. It may follow in the cachexia of malignant disease. Very exceptionally, it may be caused by a unilocular benign tumor and be cured by removal of the growth. Martin found amenorrhea 11 times in 581 ovarian tumors of all types and Lippert 19 times in 635 cases. Menorrhagia is a common symptom in intraligamentous tumors, probably from interference with the circulation. Bleeding after the climacteric occurs often in malignant disease and occasionally when the growth is benign. It may be due to torsion of the pedicle. Precocious menstruation in young children and premature sexual development may disappear after the removal of the tumor.

Sterility may result from destruction of all of the functioning ovarian tissue, or from mechanical disturbances from the size of the tumor or associated inflammation. There are many cases in which pregnancy resulted after a considerable period of sterility following removal of the tumor. Yet sterility is not the rule. Any slow-growing tumor may be found with pregnancy, even when the growth is bilateral. On the contrary, certain signs of pregnancy may be caused by the tumor. They are chiefly breast changes and consist of hypertrophy

and tenderness of the breast, increase in the pigment of the mammary areola, and the presence of colostrum.

The severity of the symptoms may depend upon the size and location of the tumor, adhesion formation, and the individual sensitiveness of the patient. Tumors may develop to most astonishing size without causing symptoms. Small tumors impacted in the pelvis, on the contrary, cause pain, vesical and rectal disturbances, all of which are aggravated by inflammation.

Occasionally, even small, freely movable tumors may cause a sense of weight in the pelvis and pain in the back and sides which radiate down the legs. Tumors bound down by adhesions are most likely to cause symptoms. Larger abdominal tumors may occasion disturbances as a direct result of their size, but not always in proportion to it. Even mammoth tumors may have surprisingly few symptoms. As a rule, however, there are symptoms from pressure. Pressure on the stomach may be responsible for anorexia and nausea and vomiting. Pressure on the intestine may cause constipation and hemorrhoids. Respiratory difficulties follow upward displacement of the diaphragm. There may be edema and varicosities of the abdominal wall, genitalia, and lower limbs from disturbances of the venous circulation. Complete prolapse may be the sequence of ascites, even in nullipara. Inguinal, femoral, and umbilical hernia are often seen. Bladder disturbances, including tenesmus and paradoxical incontinence, are quite common. Compression of the renal veins may cause albuminuria and a decrease in the urinary output. If not too far advanced, they may disappear after operation. Pressure on the ureters may cause dilatation and hydronephrosis. We have seen polyuria reduced by removal of the tumor. Many have reported glycosuria from compression of the pancreas. Bauereisen's case disappeared after ovariectomy in spite of three years' duration.

Ascites is rarely caused by pressure alone. It is usually found with the solid and, especially, with the malignant tumors. It may be due to associated renal cardiac, or hepatic changes.

Complications of Ovarian Tumors.—Ovarian tumors may undergo a number of complications. Chief of these are torsion, infarct formation and infection. We will discuss only torsion.

TORSION.—Torsion is the most common of the serious complications. To assume clinical dignity, it usually requires a turn of 180 degrees. Rokitansky, in 1840, called attention to the condition.

It is difficult to determine the frequency of torsion. Some authors report only cases giving rise to severe symptoms; others have reported all cases. Its frequency is probably decreased in recent years, since cases come earlier to operation. Mickwitz reported the remarkable frequency of 47 per cent in Kuestner's clinic, due to the fact that their patients would not seek treatment until driven by pain. Other reports

give percentages varying from 6 per cent (Martin) to 30 per cent (Jelpke). Estor recently found 7.8 per cent. Wiener, in 1915, found pedicle torsion 33 times in 269 tumors removed in the Mount Sinai Hospital in New York (12.26 per cent).

Torsion occurs most frequently in tumors of medium size which alone can rotate easily in the abdominal cavity. The very large tumors are very rarely twisted. The cysts must be free for torsion to occur. There is a difference of opinion concerning the length of the pedicle. Estor states that the shorter pedicles are more likely to twist, though Pfannenstiel believes this occurs more often in the long, delicate ones.

Torsion may occur in any type of tumor. It is most common in cystadenoma because this tumor is so much more frequent. It occurs in a large proportion of the dermoids and fibroids because of the greater weight of the tumor (Aimes) or the great length and delicacy of the pedicle (Pfannenstiel). Probably both factors are partially responsible. Torsion is unusual in malignant tumors, since they are early held down by inflammatory or neoplastic adhesions.

Torsion occurs most frequently in right-sided cysts. These tend to rotate like the hands of a clock. Tumors of the left side rotate in the opposite direction (Kuestner's law). Torsion occurs in this typical manner in from 80 per cent to 85 per cent of cases.

Causes of Torsion.—Torsion may result from external causes or internal factors working in association.

The external causes are due to sudden disturbances of intra-abdominal tension caused by coughing, vomiting, or other sudden movements of the body. Physical examination of the patient has occasionally caused it. The older writers state that laxity of the abdominal walls due to parity favored it, yet Aimes found it frequently in nullipara.

The internal factor consists in changes in volume of neighboring organs. The filling and emptying of the bladder, intestinal peristalsis, a development of a tumor in the other ovary, changes in the tumor itself, the development of different densities in various portions of a multilocular cyst, the sudden change in volume due to spontaneous rupture or puncture, the changes in size and position of a uterus in pregnancy and the puerperium, and the removal of ascitic fluid may be predisposing factors for torsion.

Other various interesting theories of the mechanics of torsion have been enumerated by Aimes, yet none of these are proved.

The uterus may be twisted along with the tumor, being turned about the lower segment of the uterus. It is especially likely to occur in children and in pregnancy. As a result of torsion, the tumor may lie on the side of the abdomen opposite that from which it originated. The number of turns varies from half a turn to six or even to ten. Hollander found a case with twenty-five complete turns. The tumor

may twist entirely away from its stalk. Twenty-five per cent of reported cases had two complete turns.

The resulting lesions depend upon the rapidity of the process and the number of turns. Changes occur both in the pedicle and the cyst wall. Thrombosis is usual and may extend even through the broad ligaments to the iliac or femoral veins. Similar arterial changes may follow the venous lesions, even in incomplete torsion. Gangrene and the slough of the tumor may follow complete torsion. The cyst is markedly congested and there may be intracystic hemorrhage which may cause death. The cyst walls are edematous and infiltrated with blood, and marked by blue-black hemorrhagic infarcts. Fibrinous deposits cover the wall and form points for adhesions. Peritoneal irritation is the rule, yet subsequent infection is a rare complication (5 per cent). Adhesions occur in 50 per cent of cases. Ascites develops rapidly, and varies according to the degree and intensity of the congested phenomenon of a clear serous fluid to almost pure blood.

The outcome varies. Death may ensue. Spontaneous detorsion is a possible but unusual result. Incomplete torsion may cause only superficial lesions with adhesion formation and the acute crisis may pass, or recurrent attacks may occur. Even gangrene need not be fatal, since a parasitic circulation may develop. As a result, the cyst may continue to live, occasionally may grow, or rarely may atrophy and be the seat of sclerotic or fatty degeneration or calcification. These favorable results cannot often be expected. There may be a sudden rupture of the vessels of the pedicle and a veritable peritoneal inundation.

Symptoms of Torsion.—These, like the pathological lesions, vary with the degree and rapidity of the twisting. Sudden torsion is supposed to occur in 28 per cent to 30 per cent of cases. There is intense pain and peritoneal reaction. The pain may cause syncope, pallor, shock, a rapid, small pulse, and cold sweats. The peritoneal reaction is marked by abdominal distention. There may be dyspnea, nausea, and vomiting, or sometimes constipation. Paralytic ileus may be a feature. True obstruction may occur when the growth has been accompanied by adhesions.

The temperature varies. Low at first, it arises as a result of absorption of blood or peritoneal infection. Metrorrhagia is important, since it may direct attention to the pelvis in an acute abdominal crisis for which no cause may be apparent. Rather infrequently, the patient is aware of a sense of displacement of an abdominal mass felt at the beginning of symptoms.

The mild subacute or chronic torsion occurs in about 60 per cent of cases. It is more easily recognized and the signs are milder and the patient is less ill. The pain is less intense and may reappear at irreg-

ular intervals or at each menstruation. The abdomen may remain tender, or may be swollen for several days after each attack.

Latent torsion occurs without symptoms in approximately 10 per cent of cases. It may be recognized only when the condition is found at operation. Gourden described a case in which the cyst was parasitic, having been detached.

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CHAPTER XIII

TUMORS OF THE BROAD LIGAMENT, THE ROUND LIGAMENT, AND THE FALLOPIAN TUBES

Tumors of the round ligament—Historical—Etiology—Age—Types—Location and size of tumors—Microscopic picture—Symptoms and clinical course—Diagnosis—Treatment—Prognosis—Tumors of the ovarian ligament—Tumors of the mesosalpinx—Cysts of fimbria ovarica—Of para-ovarium—Hydatid of Morgagni—Of accessory tubes—Fibroids of the broad ligament—Fibromyoma—Age—Appearance and form—Symptoms—Growths—Degenerations—Lipoma—Sarcoma—Treatment of solid tumors of the broad ligament—Tumors of the fallopian tubes—Classification (Polyps—Papilloma)—Treatment—Malignant epithelial tumors—Carcinoma—Frequency—Age—Classification—Symptoms—Ascites—Diagnosis—Prognosis—Treatment—Secondary tubal carcinoma—Benign tumors arising from mesoblast tissue—Enchondroma—Lipoma—Lymphangioma—Fibroma—Adenomyoma—Malignant—Sarcoma—Symptoms—Mixed tumors—Embryological tumors—Teratoma and dermoids—Frequency—Chorioepithelioma.

TUMORS OF THE BROAD LIGAMENT

Included under this heading are the tumors which occur in the round, ovarian, and broad ligaments, as well as those which lie in the mesosalpinx, but which do not develop from the tubes.

TUMORS OF THE ROUND LIGAMENT

Historical.—While a few scattered cases were noted by pathologists, the interest in this group of tumors was aroused in 1865 when Spencer Wells described two tumors of this structure which he found at operation. From this time on, isolated reports appeared in the literature so that Sanger, in 1882, was able to present his study based on his own cases and 12 which had been previously reported. This article forms the groundwork of the subject. In 1896, Cullen reported the first adenomyoma noted in the round ligament and, in 1903, Emanuel was able to collect 76 tumors of the round ligament from the literature. Taussig, in 1914, increased the number to 141, since when there has been no further compilation. In a casual review, we have found 9 isolated case reports to which we would add 3 unpublished cases occurring in our service. The group consists of 5 fibroids, 1 fibromyoma, 4 adenomyoma and 1 sarcoma.

They are reported by Iraeta, in 1917; Moench, Ward, and Cirio, in 1918; Brown, and Walther, 1919; Cullen, and Durand, 1920. Two of our cases were fibromyomata and one adenomyoma.

Types of Tumor Found.—In a review of the subject of tumors of the round ligament, one is struck by the variety of neoplasms which may occur in this simple structure, although their number is not great when compared with tumors in other parts of the body. It is well to remember, as Krusen emphasizes, that the round ligament properly must be considered as a part of the uterus, and that growths which are seen in the uterus may be seen also in the round ligament. We will follow Emanuel's suggestion and not consider hydrocele of the round ligament, since this is not really a tumor of the round ligament but is a collection of fluid in the spaces of the tunica vaginalis which is open in the embryo, but which later becomes closed off. These accumulations have only a slight connection with the round ligament and are not within its substance, as they must be to be true tumors. Lewis, in 1903, states that the following tumors have been recorded: fibroma, including fibromyoma (which is most common); fibrosarcoma; adenomyoma; cysts (simple and dermoid); and lipoma. Hematoma and abscess have been recorded, but these are not neoplasms. Two cases of carcinoma are present in the literature which are of considerable interest, since normally the round ligaments do not contain glands. The incidence of the more frequent of the neoplasms is given in Taussig's table where he records 79 fibromyoma; 30 adenomyoma; and 6 sarcoma.

Etiology.—The etiology is not known. Much work has been done to determine the histogenesis of the various tumors included in the general group. Fibroma and fibromyoma have the same origin as similar growths in the uterus. The suggestion of Handley that fibroids might arise from accessory fallopian tubes, which Kauffmann says occur so frequently, has not been well received. The etiology of adenomyoma has already been discussed (p. 163). Cysts are usually believed to have developed from the peritoneum. This view was first advanced by Opitz, and has been accepted by Emanuel, Robert Meyer, Foederl, and Vassmer. Lewis believes that the carcinomata which have been found in the ligament are due to misplaced embryological cells (Cohnheim's theory) while Dubar considers that his case developed from embryologic remnants of the wolffian body, a theory which is accepted by Opitz. Emanuel feels that it is more likely that they developed from unrecognized extensions from adenomyomata.

Nothing is known as to the predisposing causes. Lewis points out that pregnancy does not seem to have any etiological bearing. Nor has he found anything to support the older view of Sänger that traction of a displaced uterus may be a causative rôle. A review of the literature does not indicate that trauma plays any part in the origin of the tumor.

Age.—Taussig found that the majority of fibroids occurred in patients between thirty and fifty years of age, agreeing rather closely with Spencer's earlier statement that tumors of this type were more common after forty. Cullen says that the adenomyomata usually occur during the menstrual age. Taussig found that the sarcomata were described between the ages of twenty-two and forty-four. The youngest tumor in this location was a rhabdomyoma found by Aichel in a newly born child, while the oldest case was a fibroma in a woman of seventy-six, reported by Winckel.

Location of Growth.—Tumors may spring from any portion of the round ligament, and, in general, may be either intra-abdominal or extra-abdominal. The latter are more common. Emanuel, in his analysis of 80 cases, found the distribution as follows:

	Cases
Intra-abdominal	20
Extra-abdominal (inguinal canal or labial folds)	60

Nobesky found 15 intra-abdominal tumors and 38 extra-abdominal. Taussig reports 18 intra-abdominal and 30 extra-abdominal.

The intra-abdominal tumors arise most frequently from the portion of the round ligament which is nearest the uterus. They usually grow outward into the peritoneal cavity so that they present the appearance of a pedunculated tumor attached to the ligament. They may, however, grow down into the broad ligament. If situated near the internal ring, they are very likely to grow subperitoneally. Lewis found, in his review of the extra-abdominal cases, that the tumors might be situated directly over the external orifice of the inguinal canal, at the upper extremity of the labia majus, or above or below the labia majus, where normally no tissue of the round ligament can be found.

There is no agreement as to which side is more commonly involved. They may be found on either the right or left round ligament. Emanuel found more than three times as many on the right side as on the left. Spencer, in 1904, found 9 cases on the right side and 5 on the left, as well as 1 case which presented a tumor in each ligament and 1 which had two tumors in one ligament. Krusen, in 1908, stated that most of the growths occurred on the right side and in multipara. Muhlen, in 1910, collected 76 cases and found that the majority were on the right side. In 1914, Taussig found that the tumors collected and published, since Emanuel's tabulation, were 20 on the right side and 17 on the left.

Size of Tumor.—The size of the tumor varies greatly and may range from that of a small kernel to that of an infant's head or larger. Lewis found that the tumors in the inguinal canal were much smaller than those in the labia majus. Taussig reported that, as a whole, the

extraperitoneal tumors were larger than the intraperitoneal. Some of the larger tumors recently reported are as follows: Moench, 1918, a sarcoma the size of a grapefruit; Walther, 1919, a fibromyoma measuring $22 \times 17 \times 13$ centimeters and weighing 2 kilograms; Ward, 1918, a fibroid 46×48 centimeters, which weighed 3 pounds. 8 ounces; Spencer's tumor, in 1904, found in a virgin of twenty-four, weighed 6 pounds.

The form varies considerably. The fibroids and fibromyomata are usually round or oval; occasionally, they are multilocular. Owing to the frequency of cystic and telangiectatic changes, a certain proportion have a semisolid or even fluctuating consistency. Ordinarily, however, they are firm. In 19 cases, Taussig found that there was only a thin shell of fibromuscular tissue surrounding a cyst. Three of these contained blood and were classed as hematoma. Occasionally, these cysts were multilocular. The fibroids may be pedunculated or sessile, intraperitoneal, or subperitoneal. One half of the cases collected by Spencer were associated with uterine fibroids. The pedicle may be formed by the ligament itself, which has hypertrophied, or there may be a separate pedicle attaching the tumor to the ligament. Torsion of this pedicle may occur. The outline of the tumors which are situated extra-abdominally varies according to their situation, as has been discussed in fibroma of the labia (page 3.)

Adenomyoma may occur as large nodules containing cystlike spaces which may contain chocolate-colored fluid or present brown or yellow pigmented areas.

The sarcomata are small and are situated most frequently extra-abdominally.

The lipoma may be globular or elliptical and may present a smooth, or lobulated surface. Their consistency varies on palpation, depending upon the degree of tension in the tumor. Usually firm, they may be soft, elastic, or fluctuating. The lipoma may be multiple, or single; in the former instance, the growths are independent of each other.

Microscopic Picture.—The histology of the tumors of the round ligament is identical with that of the same tumors in other situations in the body. They present, moreover, various degenerations which have been described for the uterine fibroids, namely, lymphangiectatic, myxomatous, calcareous, hyaline, and malignant changes.

Symptoms and Clinical Course.—The tumors of the round ligament usually grow slowly and consequently may be followed for a considerable period without marked increase in size. Cullen reported a case of adenomyoma which had been present for eight years and Blumer recorded one which had been known to be present for twenty-two years. Maly described a myxosarcoma which had existed for sixteen years and Taussig one which had been followed for two years.

The symptoms depend upon the situation of the tumor. If located

intra-abdominally, the neoplasm may occasion little or no inconvenience. As the growth increases in size, pain may follow from pressure. At first, there is discomfort in the lower abdomen which presently changes to pain which may radiate down the legs and seriously interfere with locomotion. Pressure symptoms from the bladder and the ureter have been reported. The symptoms are usually aggravated during menstruation. Tumors in this situation do not prevent pregnancy nor cause abortion (Spencer), although pregnancy usually stimulates them to active growth (Taussig).

The symptoms of the extra-abdominal forms have been considered under fibroma of the vulva (page 1).

Diagnosis.—The diagnosis of tumors of the round ligament may be difficult. Tumors developing on the intra-abdominal portion of the ligament are usually confused with pedunculated fibroids of the uterus, tumors of the broad ligament, ovarian or para-ovarian growths, or even with pus tubes. As has been stated, under the section of fibroids of the vulva, neoplasms of the extra-abdominal portion of the ligament may be confounded with incarcerated hernias or enlargement of the lymph glands. The painful phenomena which occur at time of the menstrual periods, while fairly characteristic of fibromyoma of the round ligament, are not pathognomonic because ovarian tumors, or ovarian hernia, may give the same symptoms.

DIFFERENTIAL DIAGNOSIS.—The differential diagnosis between the different varieties of the solid tumors of the ligament can be made only by microscopic examination of tissue.

Treatment.—The treatment of these tumors is removal, which should be done as early as the tumor is recognized.

Prognosis.—The prognosis depends here, as in all cases, upon the histologic structure of the neoplasm. Relief of symptoms usually follows removal of these tumors. We must keep in mind that tumors in this region, though benign at first, may undergo malignant degeneration and thereby render the malignant process more serious. Sarcomata are rare and we find record of only 7 where the diagnosis is definite. Without exception, they were slow-growing and but slightly malignant clinically. None of them had given rise to metastases, nor is there record of recurrence after operation.

There are only two deaths following operation for sarcomata. The first case was recorded thirty years ago by Sängner, and was a fibrosarcoma in which the incorrect diagnosis aided in the unfortunate result. The condition was believed to be a hernia and the patient wore a truss for four years, at the end of which time she complained of the utmost pain and a tumor the size of a child's head. The growth was now considered a fibrocystoma but operation revealed the presence of a fibrosarcoma. The details of the death of Moench's case are not given, other than that it followed eight weeks

after a sarcomatous growth the size of a grapefruit which clinically was felt to be extremely malignant but which was thought to be completely removed.

Para-ovarian Tumors.—In the female, the para-ovarian, or organ of Rosenmüller, represents the fetal remains of the mesonephros, and is situated between the leaves of the broad ligament, near the tube and ovary. It consists of a main channel (the duct of Gärtner) and eight to ten lateral branches, or vertical tubules, which converge in the direction of the hilum of the ovary. The duct of Gärtner usually ends blindly between the two layers of the broad ligament; occasionally, it is continued downward in the wall of the uterus and vaginal fornix and may give rise to cysts in these regions. The lateral end of the duct is converted into a blind pouch which frequently becomes enlarged and cystic and is known as the hydatid of Morgagni (page 390). The para-ovarian reaches its highest state of development in sexual life, although its exact function is unknown; various experimental data has been accumulated which tends to support the view that the structure furnishes an internal secretion.

Para-ovarian Cysts.—Para-ovarian cysts develop from the vertical tubule and are the most common tumor of this structure. As small structures they are very frequent and are usually noted during operations for other conditions. Larger sacs are found less frequently. According to Olshausen, they were found in 11.3 per cent of his ovario- and para-ovariotomies. Veit found the condition in 11.8 per cent of his material, Schauta 9.1 per cent, Lippert 6.7 per cent, Martin 14.4 per cent. Kelly, in 410 cases of cystic tumors of the ovaries of all kinds, found that para-ovarian cysts occurred in about 12 per cent. As a rule, para-ovarian tumors occur about middle life. According to Kelly, the average age was thirty-nine years. As before mentioned, the cysts are usually small, although they may reach a considerable size, as is shown by Kümmell's case of forty-two pounds, Nagel's tumor containing thirty-three liters of fluid, and Mayo Robson's of one hundred and five pounds.

Para-ovarian cysts are generally unilocular. In the smaller cysts, however, two or more loculae may occur. The larger cysts are almost always unilocular. The tumors may be bilateral (small cysts), but the larger cysts are nearly always unilateral. The cyst wall is usually flaccid, in marked contrast to that of ovarian tumors.

Para-ovarian cysts originate between the folds of the broad ligament, and the peritoneal coat is freely movable over the tumor. As the cyst grows, it presents either as a pedunculated tumor which lies free in the abdominal cavity, or one which burrows down between the layers of the broad ligament and develops extraperitoneally in the abdomen. The latter type usually displaces the uterus from the pelvis. The cysts are pearlish gray, or pinkish in color, and histologically are

composed of three layers: (*a*) a serous coat derived from the broad ligament; (*b*) a middle layer of fibrous tissue in which a few muscle bundles are scattered; and (*c*) an inner layer of cylindrical, often ciliated, epithelium. The form of the epithelium depends upon the amount of pressure exerted by the fluid; thus the epithelium may be high columnar or else flattened and containing desquamated and degenerated cells. Papillary fibro-epithelial growths from the cyst wall are often seen. The cyst contents are usually thin and opalescent, but may be changed to a thick brown color as a result of hemorrhage, or fatty degeneration usually caused by torsion of the pedicle. The relations of the tube and ovary to the cyst are characteristic. The tube is drawn out and arched up over the upper surface of the tumor and its fimbriated end is adherent to the cyst. The ovary is found as a small flattened prominence on the under or anterior surface of the cyst wall. The tube may be stretched to enormous length. Payer cites a case in which it measured 76 centimeters. When the cyst develops directly under the tube, the fimbria may be so stretched and separated from the ovary that it may be definitely said to cause sterility.

SYMPTOMS.—Symptoms usually develop only when the tumor has attained considerable size unless complications have ensued. They are not likely to occur early when the growth is pedunculated and movable, since this form early leaves the pelvis and rides free in the lower abdomen. Pressure symptoms may develop early when the tumor is sessile and grows between the leaves of the broad ligament. The patient then complains of a sense of weight and fullness in the pelvis, pain in the hips and thighs, and difficulty in micturition and defecation. Yet symptoms result more frequently from torsion which, unfortunately, is very common. The symptoms following torsion are identical with those of ovarian cysts, namely, acute lower abdominal pain and sudden enlargement of the tumor. The picture varies, depending upon the completeness of the strangulation and the time when it occurred, and varies from simple congestion to gangrene. Adhesions to the intestine often result and are the cause of symptoms. The cyst may become infected through the bowel wall which is adherent to the gangrenous cyst. Adhesions between the cyst and small bowel may readily cause intestinal obstruction.

DIAGNOSIS.—The symptomatology of para-ovarian cysts is by no means characteristic. The diagnosis is not often made until the abdomen is opened because para-ovarian cysts cannot be differentiated from cysts of the ovary unless the ovary itself can be felt distinctly apart from the smooth semifluctuant tumor.

TREATMENT.—Cysts of appreciable size should be removed as soon as possible, since their early recognition permits conservative surgery. Salpingo-oöphorectomy is seldom necessary in moderate-sized cysts, either when the tumor hangs free or is imbedded in the broad ligament.

Yet proper peritonealization is the secret of ultimate good results and one should never leave raw surfaces in the desire to do conservative surgery. Early operation before the advent of torsion alone promises the possibility of successful conservative work, since radical measures are often indicated in the presence of the sequelae of torsion of the stalk.

PROGNOSIS.—The prognosis is good in uncomplicated cases. The tumor does not return. If all raw peritoneal surfaces are turned in, there should be no adhesions.

Para-ovarian Tumors Other Than Cysts.—Tumors which fall into this classification are very rarely seen. They are counted as the most infrequent tumors in pelvic pathology. Besides the papillary cysts which have just been mentioned, there have been reported a few cases of a grapelike cystoma (Werth). Adenomyoma and fibro-adenoma have been described by Pick and Bennet. Carcinoma of the para-ovarium have been observed by Sängner, Werth, R. Meyer, and Schottlaender. The latter's case presented as a metastatic growth from a uterine carcinoma which was implanted in the wall of the para-ovarian cyst. Tabney reported a case which presented cancerous growths in both para-ovaria which were metastases from a primary carcinoma of the stomach. Werth has described a primary adenosarcoma.

Cysts of the Hydatid of Morgagni.—The hydatids of Morgagni are cystic dilatations of the blind end of Gärtner's duct. They are occasionally converted into small cysts, pedunculated and translucent, which contain a thin serous fluid. They are regarded as retention cysts and are usually attached by long, slender pedicles to the fimbria of the tube or the peritoneum of the mesosalpinx immediately beneath them. They are seldom larger than a centimeter in size, although rarely they attain the dimensions of a walnut. They have no pathologic significance, unless there is torsion of the pedicle when they may cause symptoms. We have seen a case which simulated an ectopic pregnancy.

Cysts from Accessory Fallopian Tubes or Ostia.—Cysts not infrequently arise from inclusions of occluded accessory fallopian tubes. The tubes presenting these growths are small and poorly developed yet may reproduce in their structure the essential histologic elements of a normal tube. They may be provided with a patent ostium which opens into the peritoneal cavity, or the ostium may be blind. There is considerable discussion as to the histogenesis. Hydrosalpinx of an accessory fallopian tube was first described by Kossmann. Handley demonstrated a broad ligament cyst which had sprung from an accessory tube. These tumors may grow to considerable size. Collingsworth, in 1903, removed at operation a hydrosalpinx of an accessory tube which measured three inches in diameter. It had caused much pain.

Solid Tumors of the Broad Ligament.—In addition to the new growths which arise from the embryonal elements in the broad ligaments, and are cystic in character, there are a group of solid tumors of mesodermic origin. For the most part, these are secondary from the extension of primary tumors from the round ligament, uterus and ovaries into the substance of the broad ligament. These have been discussed in their proper classification.

The primary solid tumors of the broad ligament include fibroids, lipomata, and sarcomata.

Solid tumors may develop in the broad ligament as a primary process, or may grow into it by extension from other structures. The latter have been considered under their proper headings. The primary tumors consist of fibroids, lipoma, sarcoma, and dermoids.

The tumors which develop as primary processes may be located anywhere in the broad ligament. Those which develop in the upper portion come to occupy a position in the pelvis similar to tumors of the uterine body, the round ligament, and ovaries from which they may be distinguished with difficulty before operation. The neoplasms which develop near the base of the broad ligament usually grow downward and eventually tend to block the pelvis.

Fibromyoma.—The majority of these tumors lying between the folds of the broad ligament are extensions from uterine fibroids, yet this class never separate from the uterine wall, as may pedunculated subserous growths, and present as free structures. Careful examination always discloses connecting muscle and fibrous bands. A smaller group of tumors may develop as independent structures, arising from fibromuscular bands in the subserous cellular space, since the same factors which produce fibroids in the uterus exert their influence in the broad ligament. Fibromyoma primary in the broad ligament are seldom seen when the uterus is perfectly normal. The very great majority occur when the uterus is also the seat of fibroid changes. The first case was reported by Burnham in 1867. Since then, there have appeared a few isolated reports so that, in 1907, Vance was able to collect only 16 broad ligament fibroids which were deemed to be independent of uterine growth, 12 of which were reported in America. Doran, in a later review, compiled 32 cases.

Age.—The age of the patients in Vance's series ranged from twenty-two to fifty-six years. Of these, three were under thirty and two over fifty years. Six of Doran's cases were under thirty and six above fifty years. From these figures we see that most of the cases occur between thirty and fifty years.

Appearance and Form.—The size varies from very small growths to enormous tumors—one case weighing forty-four and a half pounds. Spencer enucleated a tumor of fourteen pounds from the broad ligament nine hours before delivery at term. The tumors may be single,

or multiple. They are rarely noted as bilateral growths. Thierry, in 1906, reported a bilateral growth. Eising reported another in 1911 which, together with the uterus, constituted a mass measuring $7\frac{1}{4} \times 4\frac{1}{4} \times 3\frac{3}{4}$ inches.

Most of the fibroids of the broad ligaments are sessile tumors, but Vance collected 9 cases which were pedunculated. Nearly all of these are supposed to have developed from the ovarian ligament, yet there is always a possibility that some arose from the fibrous tissue in the depth of the broad ligament and are identical from the standpoint of origin with tumors which project through the obturator foramen and sacrosciatic notch which have been discussed under fibroids of the vulva (page 1). Vance's case was a vascular growth of twelve and a half pounds which had no connection with the normal uterus. Bevers, in 1909, reported two pedunculated growths which developed from the ovarian ligament and had undergone torsion.

The outline of the tumors is identical with that of fibroids in other parts of the body. Their surfaces are irregularly rounded, depending upon their position.

Growth.—As a rule, the tumors grow slowly, since they are usually of fibrous tissue. Soft myomatous tumors grow faster. The growths have been known to be present from one to twenty years before removal.

Degenerations.—The same degenerations observed in uterine fibroids may occur with fibroids of the broad ligament.

Cystic degeneration is a rather common occurrence. As a rule, the cysts do not attain great size, yet McNeile's case in 1909 contained ten quarts of clear straw-colored fluid.

Hyaline degeneration has been frequently described. Two cases of Vance's series presented extensive areas of calcification.

Adenomyoma.—Some of the cystic tumors which have been described as cystic fibroids are undoubtedly adenomyomata which may develop as primary processes according to von Recklinghausen's theory of origin from wolffian remnants or as secondary processes from the rectovaginal septum, cervix, uterus, tube or round ligament. They have been described under their proper heading.

Symptoms.—The symptoms of fibromyoma of the broad ligament are variable, but essentially they are like those of uterine fibroids. Pain is the result of pressure or of adhesions. When the uterus is normal, there need be no disturbance of menstruation. Symptoms, as a rule, develop gradually and may be present for many years. McNeile's case has given symptoms for more than ten years. In an unreported case seen by one of us, symptoms had been present for five years before they were sufficient to force the patient to seek relief with a tumor the size of a fetal head. The slow growth of the tumor is a distinguishing feature.

Lipoma.—Lipoma of the broad ligament is rare. Lockyer, in 1919, was able to collect only 7 cases. In 2 of these reported by Borrmann the round ligament dwindled away as it passed over the fatty tumor, suggesting that the neoplasm might be associated with an arrest in development of the round ligament. Lockyer reported a case associated with an ovarian dermoid cyst. It lay in the base of the mesosalpinx, was encapsulated and severed from the cyst wall. Emrys-Roberts described a case in which the tumors were situated in the broad ligaments immediately below the posterior part of the fimbriated ends of the fallopian tubes. They were discovered accidentally during the pathological examination of a specimen of ovarian fibroid complicating uterine fibroids.

The size varies tremendously. Emrys-Roberts' case presented as two bean-sized nodules. One of Borrmann's measured 7.5x6.5x4 centimeters. It was bilobed. Bland Sutton and Giles cite one which reached as high as the navel and weighed 5 kilograms. One of the tumors described by Emrys-Roberts contained two small clear cysts lined by columnar epithelium which the observer believed indicated an origin from Kobelt's tubules.

The tumors are encapsulated, nonadherent, and therefore are easily removed.

Sarcoma.—Webster states that primary sarcoma of the broad ligament is extremely rare and is usually discovered only when the condition is inoperable. According to Bland Sutton, it is usually of the spindle-cell type and rapidly growing. There is no doubt but that a considerable proportion of cases in the literature adduced as primary sarcoma may equally well be regarded as secondary extensions from a process primary in the ovary, since many of the cases are so late when seen that the anatomic relations cannot always be precisely determined. There is no doubt, however, but that the tumor can develop from aberrant ovarian tissue situated in the broad ligament. Such a case was described by Outerbridge, in 1919, in which there was a cystic sarcoma the size of an adult head in the broad ligament of a girl of nineteen. The ovary was not involved, although the tumor was adherent to the intestine. Cystic degeneration was present. Microscopically the tumor exhibited the typical picture of a spindle-celled sarcoma of a somewhat fibrosarcomatous type containing areas suggesting the structure of ovarian stroma. Davies, in 1914, reported a case in which the landmarks were more definite. The tumor was walnut size, situated in the base of the broad ligament of the right side at the level of the cervix. It bulged into the vagina and caused pain. It proved to be a typical spindle-celled sarcoma. The uterus and adnexa were normal. The tumor recurred four months after removal and five months later reached almost to the umbilicus.

Dermoids.—Dermoids of the broad ligament are rarely seen. They originate in the subserous cellular tissue and present the same characteristics observed in ovarian dermoids. A few cases have been seen in pelves presenting normal ovaries. There are several theories advanced to explain their origin. The majority believe that they develop from aberrant ovarian tissue which has been included within the folds of the broad ligament. Others hold that they arise from an impregnated egg from which one of the original cell elements has been extruded and exists as a fetal inclusion as a fetus within a fetus (blastomere). Others see the growth as an expression of misplaced germ cells which develop parthenogenetically. A few consider that they represent defective twin development.

Since the tumors usually develop in the depth of the broad ligament, they tend to grow downward, pushing the pelvic structures to one side. Cases have been described in which they have been extruded from the ischiac fossa to appear under the skin of the buttocks. Freund states that they may vary in size from a pigeon's egg to that of a fetal head.

Their shape is more or less oval, depending somewhat upon the pressure which is exerted upon them, since they are more or less flaccid in structure. The histologic picture is similar to that of dermoids of the ovary. The fluid contents of the tumor may be nondistinctive or contain the characteristic sebaceous or atheromatous material with or without hair or teeth.

Broad ligament dermoids grow very slowly and their symptoms depend almost entirely upon pressure disturbances. Occasionally, they become infected.

Treatment of Solid Tumors of the Broad Ligament.—Since the exact nature of the growth cannot be determined before operation, the tumor should be removed as soon as its presence is known, because of the chance of malignant degeneration. This rule holds true even in the absence of symptoms. Often the neoplasm can be shelled out of the broad ligament leaving the other structures intact. The larger growths may be removed only after hysterectomy because of the vascular field.

TUMORS OF THE FALLOPIAN TUBES

Tumors of the tubes may develop from embryonic elements included in that structure or from secondary degeneration of its adult tissues. For the purpose of study, we will divide them according as they arise from epithelium or mesoblastic tissues. Teratoma and dermoid are considered under the head of embryoma. The tumors may be cystic or solid. The cystic swellings on the surface of the tube result, as a rule, from inflammatory conditions. Under the head of

solid tumors are included nearly all true neoplasms of the tube. They may be benign or malignant.

Benign Tumors of the Tubal Epithelium.—This group is composed of polyps and papilloma.

POLYPS.—There is considerable controversy as to whether the cases reported as polyps are true neoplasms analogous to similar formations in the cervix and body of the uterus. The 6 cases which have been reported (Beck, Breslau, Leopold, two cases; Wyder, and Huffmann) have all been associated with pregnancy and were recorded in the older literature. All of them exhibited decidual changes and most of them were thought to have caused the arrest of the ovum and to have been responsible for the rupture of the tube in the ectopic pregnancy. They had not presented symptoms.

PAPILLOMA.—The papilloma are villus or cauliflower growths which arise from the endosalpinx. They were first described by Doran, in 1879, as "exuberant morbid growths which lie in the interior of the fallopian tube." Doran regarded them as of inflammatory origin.

They are very rare tumors. Lockyer, in his critical review, accepted but 16 cases.

Etiology.—The majority of investigators who have reported cases support Doran's view that the condition is a papilloma which has developed upon an inflammatory basis. While there is some exception to this theory, it is a fact that in nearly all of reported cases, there had been preceding salpingitis.

The ages of patients presenting this condition ranged from thirty-nine to fifty years in the series collected by Sanger and Barth.

Appearance and Form.—The size of the tumor varies. It may range between that of an orange and that of a small melon. The tube is not only distended by the tumor but by a considerable amount of fluid. Sometimes the latter is so great as to constitute a hydrosalpinx. The growth may form a rounded or elliptical swelling in the outer portion of the tube. Between it and the uterus, the tube may appear unaltered. The tube is usually enveloped in firm adhesions. The mass may lie in the true pelvis or in the lower abdomen.

The tumor may present as villus and papillary types (Macrez). In the former, the growth exhibits long cylindrical or conical processes. The papillary form is a more advanced stage of the villus type and results from proliferation of the slender villi. Ulceration and necrosis are not present in the benign papilloma. This distinguishes them from the malignant papilloma of the tube.

The fimbriated portion of the tube may be closed, in which case the tube assumes the form of a cyst. On the other hand, both the uterine and fimbriated end may be closed or the fimbriated end may be the only patent extremity. The fluid contained in the tube has been studied by Macrez, Doran and others, and is found to vary from a thick, mucous

or syrupy fluid to a thin, pale, serous material. Macrez emphasizes that an admixture of blood is a sign of malignancy.

On microscopical examination, the tumor is composed of papillae which arise independently from the wall of the tube. The excrescences are invested by a single layer of columnar epithelium which may or may not show cilia. The folds of the tube are obliterated and are replaced by the outgrowths. The mass is vascular. At the base of the papillae, the stroma cells are usually but not invariably crowded together. Their nuclei stain deeply. Hyaline and occasionally mucoid degenerations are present in the apex of the mass. There are no signs suggestive of malignancy.

Symptoms.—These are not constant. They depend often upon the patency of the tube, its location and the presence of adhesions. When the uterine end of the tube is patent, and the fimbriated end is closed, fluid escapes through the uterus into the vagina. The discharge is intermittent and results only when a certain fluid pressure has been reached in the tube. The discharge is accompanied by pain and temporary disappearance of the swelling. When the uterine end of the tube is closed, but the fimbriated portion is open, the fluid may escape into the peritoneum and irritate it so as to cause ascites. A large tubal cyst may form when both ends of the tube are closed.

The ascites is not an essential feature of the growth. It may not be regarded as evidence of malignancy, since the fluid from the tube excites the peritoneum to considerable secretion. It is believed that a small amount of fluid forced from the tube into the peritoneal cavity is the cause of an irritative peritonitis resulting in dense adhesions.

Treatment.—Because malignant papilloma are far more common than the benign growths in the tube, the removal should be radical and include the uterus, and both adnexa.

Prognosis.—The prognosis is good.

Carcinoma of the Tube.—Carcinoma of the tube may be primary or secondary. Both forms are extremely rare. The first case of primary carcinoma of the fallopian tube was described by Orthmann in 1888. Other cases were soon reported, so that Peham, in 1903, was able to collect 63 cases in the literature. Since then, there have been various tabulations every few years. In 1914, Vest collected 132 cases. Lockyer, in 1917, found 4 other cases in the literature.

The rarity of the disease is emphasized by all students of the question. Norris states that carcinoma of the tube is a hundred times as rare as carcinoma of the uterus. Vest states that there were only 4 cases of tubal carcinoma in 19,000 patients treated in Kelly's clinic in Baltimore. Hurden reports that there had been but 3 cases of primary tubal carcinoma received in the gynecological laboratory of the Johns Hopkins Hospital as against 400 uterine carcinoma. Norris, in his report which included the material from the University Hospital of Pennsylvania found only 1 case of primary carcinoma of the tube

in 2,020 gynecologic specimens. In the material were assembled 8 secondary carcinoma of the tube, 5 of which were from growths which were primary in the ovary and 3 primary in the uterus.

ETIOLOGY.—The etiology, as in carcinoma in general, is not known. The majority of students of the question have contented themselves with a search for predisposing causes. These center about inflammation and pregnancy.

Tubal carcinoma arising in tuberculous tubes have been described by von Franqué, in 1911, Lipschitz, in 1914, and Lady Barrett, in 1916. Lipschitz has collected 26 cases seen in association with salpingo-oöphoritis. Säger and Barth and others have urged sterility and single pregnancies as indicative of previous inflammation. Doran believes, however, that the carcinoma may develop independently. Vest states that 43 per cent of his collected cases gave no history of a previous pelvic inflammation. On the contrary, it is well known that tubal inflammation may result without definite clinical symptoms. The question of preëxisting salpingitis must be settled by the microscope. While not absolutely conclusive, there is much reason to believe that cancer of the tube, as cancer in general, is not likely to develop in absolutely normal tissues.

Many have urged that pregnancy and resulting puerperal morbidity are predisposing causes, yet the evidence does not appear convincing. Vest stated that 70 per cent of his series had been pregnant. Of the 79 parous women, 28 per cent had borne one child only. Lockyer sanely calls attention to the fact that such data, without controls, or the percentage of the total female population that have become pregnant, cannot be studied critically.

AGE.—The age of the patient has ranged between twenty-seven and seventy. Fifty-three per cent of Vest's series occurred between the ages of forty and fifty, at a time when malignancy is most likely to develop in other parts of the body. The data concerning the age is presented in the following table:

Age	CASES	
	Doran	Vest
27-30	3
30-35	3
35-40	4	11
40-45	8	30
45-50	30	38
50-55	18	19
55-60	18
60-65	4
65-70	1

CLASSIFICATION.—The disease may present as papillary carcinoma or papillary alveolar (adenocarcinoma).

PAPILLARY CARCINOMA OR MALIGNANT PAPILLOMA.—It is difficult to determine the relative frequency of the various types of growths, since definite data is often lacking as to reported cases. In Vest's table, 29 cases were described sufficiently accurately to allow classification. Twelve of these were malignant papilloma. Lockyer feels 3 others should be added. The majority believe that papillary carcinoma are more common than adenocarcinoma and arise from conversion of benign forms. Histologically, a malignant papilloma shows invasion of the tubal wall by proliferating epithelium. The epithelial investment of the papillae also shows marked proliferation and metaplasia. Areas of necrosis and cystic spaces are common.

ADENOCARCINOMA.—This type is more uncommon. Only 4 of Vest's table of 29 cases were definitely classified as adenocarcinoma. Lockyer adds 3 others. The tumor presents a smooth, yellowish or whitish gray cut surface. The consistency varies, since the tumor mass may be soft or quite dense. The epithelial masses may be distinguished from the fibrous stroma on careful inspection. Under the microscope, one obtains the characteristic appearance of adenocarcinoma. Areas of round cell infiltration are frequently found on the advancing edges.

EXTENSION AND METASTASES.—Veit states that pure papillary carcinoma is long confined to the interior of the tube and does not invade the wall until late in the disease. This type frequently spreads to the ovary. On the other hand, the adenocarcinoma early penetrate the wall and occasionally may rupture the serosa, through which they spread to the peritoneum and omentum. The retroperitoneal lymph glands may be involved through the lymphatics. This occurred in 7 of 43 of Stolz's cases. Peritoneal metastases have been described by Novy, Kehrler, and others. Cullen has recorded metastases to the stomach and rectum. The liver (Tonyos), the bladder (Doran), the skin (Baisch), supraclavicular lymph glands (Rossinsky), vagina (Spencer), and the diaphragm (Vest) have been the seat of metastases. The uterine mucosa may be involved by secondary implantations, as may the uterine wall by lymphatic drainage. Implantation metastases following operation have been reported by von Rosthorn and Osterloh.

SYMPTOMS AND SIGNS.—Unfortunately, there are no characteristic symptoms of tubal carcinoma. Vest states that the fact that this neoplasm appears so frequently at the time of the menopause tends to mask the true nature of the disease. The usual symptoms are the following: (1) a watery vaginal discharge; (2) abdominal pain; (3) alteration of menstruation; (4) ascites; (5) cachexia; (6) tumor.

Discharge.—A watery discharge presented in 27 per cent of cases collected by Doran. It may be continuous or appear in gushes. Usually watery and yellow at first, it later becomes bloodstained and even hemorrhagic. The periodic discharge is often accompanied by abdominal pain. The presence of a sanguineous discharge and tubal swelling is highly sug-

gestive of malignant disease of the tube. Quite naturally, a discharge may occur only when the uterine end of the tube is patent.

Abdominal Pain.—Pain was present in 53 per cent of the cases reported by Doran. It may be generalized throughout the abdomen or limited to the pelvis. It frequently radiates to the back and down the sides. The pain may be colicky, such as occurs with acute torsion of an ovarian tumor, or may be constant and dull, with a feeling of discomfort and weight in the pelvis. There may be a close connection between the pain and the vaginal discharge. Severe attacks of pain in women with chronic salpingitis should suggest the possibility of tubal carcinoma.

Menstrual Disturbances.—Dysmenorrhea is not as common as menorrhagia or metrorrhagia. Vaginal bleeding may occur in women who have passed the menopause. Yet menstrual disturbances may be indefinite and vague, and of little value as far as statistical purposes are concerned.

Ascites.—Ascites is common in late growths. It is generally ascribed to reactions of secondary deposits in the peritoneum, since the ostium through which irritating fluids could escape was open in only 1 per cent of cases. Occasionally, it is present in large amounts. Two gallons were removed at operation in Le Count's case.

Cachexia.—Cachexia is usually a late symptom as is common in all malignant disease. It may be out of proportion to the symptoms which have been present.

Tumor.—Tumors of considerable size may cause enlargement of the abdomen. They are accompanied by ascites. They are usually quite fixed and may give symptoms of incomplete intestinal obstruction. Often, however, there is no abdominal swelling. Even by bimanual vaginal examination, nothing more than an indistinct resistance may be met in the vaginal fornices. This may be further masked by the presence of ascites.

DIAGNOSIS.—There are no characteristic symptoms or signs of tubal carcinoma. The condition may be suspected when there is a tumor in the lateral pelvis in a case presenting a history of a previous tubal inflammation, a sanguineous watery discharge, especially if it is intermittent and accompanied by abdominal pain. A soft, rounded swelling in one or other of the broad ligaments and the presence of ascites will make the diagnosis more likely, but it may be difficult to exclude an ovarian or tubo-ovarian cyst. The former was noted 11 times in Doran's series of cases as an accompaniment to the cancer. Tubo-ovarian cysts were found as a complication in 26 cases tabulated by Lipschitz. When the tumor is firm, it may be readily confused with a fibroid. The latter was observed in association with carcinoma of the tube 9 times in Doran's series of cases. Occasionally, there may be neither signs nor symptoms of the growth which may be so small that its true character can be revealed only with the microscope.

TREATMENT.—The treatment is panhysterectomy and the removal of both adnexa. If a tube is removed supposedly for hydrosalpinx and found

to be cancer, the other tube and ovary and the uterus should be removed immediately. The primary mortality in Doran's collected cases was 6 per cent.

PROGNOSIS.—The prognosis is not good. Only 4 cases survived the five-year period of cure in the cases that were followed in the complete series collected by Vest. The majority of recurrences develop in the first year. Doran checked the post-operative results in 40 cases, 10 of which were dead or dying within six months to a year after operation. Giles found 10 recurrences soon after 21 operations. Stoltz states that alveolar growths recurred sooner than the papillary forms.

Secondary Carcinoma of the Tube.—The tube may be involved secondary to uterine or ovarian cancer. Kundrat's figures show the relative frequency of the involvement of the tube in carcinoma primary in the uterine body and cervix. The tube was involved 3 times in 24 fundal carcinoma and not at all in 80 cases of cervical cancer. Taussig, in 1907, recorded a carcinoma of the tube and ovary secondary to a cervical cancer. The tube is invaded usually early in ovarian cancer and late in uterine carcinoma. The organ may be invaded by implantation upon the serous or mucous coats or by the lymph stream to the wall of the tube. The tube may be invaded during the general peritoneal spread of cancer from the upper abdomen.

Benign Tumors of Mesoblastic Origin.—**ENCHONDROMA.**—Small cartilaginous tumors occasionally have been described as arising from the tubes. Many consider them allied to the embryoma. They tend to project into the lumen and occlude it. Outerbridge felt that his tumor was a causal factor in a tubal pregnancy.

LIPOMA.—Only 2 cases of lipoma are described in the literature. Parona's case was reported in 1901. It weighed three ounces and appeared to surround and infiltrate the tube. Doran described a small, fatty tumor in the ovarian fimbria hanging by a distinct pedicle.

LYMPHANGIOMA.—Leighton, in 1912, collected 4 cases and reported one other. They are all small, about the size of a large pea. On microscopic examination, the tumor is composed of loose connective tissue filled with cavities or crypts, lined by a single layer of epithelial cells. All the cases occurred with uterine fibroids.

FIBROMYOMA.—These are rare tumors. Auvray, in 1912, exhaustively studied 29 cases. Rudolph, in 1898, reported one pure fibroma. Fibromyoma may arise from any part of the tube. Occasionally they project from the ovarian fimbria. They are almost always unilateral and usually single. Ordinarily small, they may attain considerable size. Auvray's case weighed 2,800 grams.

Tubal fibroids may be subperitoneal, interstitial, or submucous. The former is the most common.

Neither the size nor symptoms are characteristic. They are usually mistaken for uterine fibroids. Their treatment is removal.

ADENOMYOMA.—There is considerable discussion as to whether there is such a primary condition. The majority of cases reported as such are now considered salpingitis isthmica nodosa.

Malignant Tumors of Mesoblastic Origin.—**SARCOMA.**—Sarcoma of the tube is a very unusual condition. There are only 8 cases reported as primary tumors, the cases of Gottschalk, Janvrin, Jacobs (2 cases), Jones (3 cases), and Scheffzek. Quénu and Longuet, and Doran have reviewed the literature.

MIXED TUMORS.—These consist of embryonic connective tissue and cylindrical epithelium. Six cases have been reported as carcinosarcoma.

PERITHELIOMA.—Perithelioma are extremely rare tumors. Gosset's case weighed one and a half pounds. Müller describes a case in which there were tumors of both tubes.

Embryonal Tumors.—**DERMOID CYSTS AND TERATOMA.**—These occur extremely rarely. Lockyer describes a teratoma and collects 6 others. They range in size from small nutlike masses to tumors the size of a fetal head.

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CHAPTER XIV

MAMMOTH OVARIAN TUMORS

Historical—Frequency—Complications of—Types of fluid—Symptomatology—Age—Prognosis—Résumé of cases.

Historical.—The subject of mammoth tumors forms a chapter of peculiar interest in ovarian pathology. In view of the natural human curiosity concerning things unusual, it is rather remarkable that no one has yet made a collection of these cases which even approaches completeness.

Gould and Pyle, in their extensive compilation of unusual cases in medicine published in 1897, mention only 7 cases in which the weight of the tumor exceeded 100 pounds. The largest of these weighed 182 pounds (Reifsnyder's case). Bullitt, in 1900, collected 25 cases over 100 pounds, and later authors have added isolated cases to this review. Brunner, Idazewski, and Zacharias each include a bibliography with their reports going more extensively into the foreign literature. Fay, in 1908, reporting a tumor which weighed about 175 pounds, without attempting to make his bibliography exhaustive, was able to find reports of 38 cases over 100 pounds; of these, 14 weighed between 150 and 200 pounds, and 5 over 200 pounds.

A more careful review of the literature gives us records of 87 cases weighing over 100 pounds, and in addition there were found records of 103 cases where the weight was between 60 and 100 pounds. Of the 80 cases, there were 21 between 150 and 200 pounds, 9 between 200 and 300 pounds, and 1 over 300.

The geographical distribution of these cases is of some interest. Thirty-seven were reported from the United States, 5 from South America, 7 from England, 11 from Germany, 10 from France, 3 each from Belgium and India, 2 each from Switzerland and China, 1 each from Italy, Austria and Holland. The Russian literature, much of the Dutch and parts of the Chinese and Indian were not available. Very possibly these contain some cases large enough to include in our review, yet it is impossible to judge this from the titles of articles, as even a 50-pound tumor would seem enormous to one who had never seen one which was larger.

Spencer Wells' first series of 1,000 ovariectomies contained only 1 tumor which weighed over 100 pounds. This weighed 125 pounds,

but this patient came from the Argentine to be operated upon by Wells. The other large cases in this series weighed 81, 78, 77, 75, 72 and 63 pounds respectively; all the others were below 60 pounds. The average weight in Wells' first series of 500 cases was 20.3 pounds.

In spite of the fact that most tumors are operated upon nowadays long before they attain any such enormous size, we find that 27 or nearly one-third of the total number of cases in this series have been reported since 1900. It may be that the greater rarity of large tumors prompts us to record a larger proportion of such growths. Yet Spohn's 328-pound case, reported from Texas in 1905, would have been remarkable enough to record in any age, as would Tuffier's 94-liter case published in 1906, or Pfaehler's 97 kilogram growth in 1904. Peaslee in his monograph on "Ovarian Tumors" in 1872 states that "the largest amount of fluid in an ovarian tumor which has been recorded is 160 pounds, which was drawn off during an operation of ovariectomy by Kimball, more than 20 pounds being still left because he could not complete the operation." He was evidently unfamiliar with the 2 very much larger cases in European literature which are mentioned in Gallez's work of 1873, namely, Martineau's 216-pound case and Adelman's 214-pound case. Emmett, in 1879, stated that "Dr. Keith had removed a tumor weighing 120 pounds, the largest ovarian tumor ever removed successfully from the living body." Nor, as we might suppose, do all the present-day cases come from remote districts. Ward's 222-pound case was a resident of San Francisco. Smith's 192-pound case had received the benefits of electricity and "Christian Science" in Boston for two years prior to her operation. Franz's 160-pound case, operated in 1916, had lived for years almost in the shadow of one of the larger Berlin hospitals.

Two methods of arriving at the weights of these larger tumors are commonly used, yet both are subject to certain inaccuracies. The first adds the weight of fluid removed to that of the sac; and, when accurately controlled, this method is entirely reliable. But fluid is frequently lost at the time of operation and the exact amount is difficult to determine. In other cases, as in those of Spohn and Barlowe, the patients were tapped one or more times for a number of days before final removal of the tumor. In such cases, the amount of fluid due to re-accumulation is of course unknown. Yet Peaslee, speaking from cases which were treated only by repeated tapings, considers two pounds a day a very rapid rate of re-accumulation, and possibly this factor is of minor importance. In many of the older case reports, where the tumors were merely tapped, the weight of the fluid only could be obtained; in these we must either accept the author's estimate of the weight of the sac or exclude the case from the series. The weight of the sac may be considerable—up to 50 pounds.

The other method commonly used subtracts the weight of the

patient after operation from her weight previous to it. It is, however, rarely possible to weigh a patient immediately after operation. At a later time, her loss in weight from edema or her gain in weight from improved nutrition are factors that must be considered, though fortunately they usually counterbalance each other. Ascitic fluid occurs so rarely that ordinarily it need not be considered. Twenty-five pounds, however, would probably be a very liberal estimate of the error by any of these methods of determination. This becomes a comparatively small factor when we consider the enormous weight of the larger tumors.

Due to the variation in shape of the abdomen, the circumference in these cases varies. It is usually greater than the height of the patient; in all the larger tumors it was considerably over six feet. The graphic description given by Spohn may convey a better idea of the size than any measurements. "The tumor came almost up to her chin and extended midway between her knees and feet. When she lay on her side on a three-quarter bed, it had to be supported on two chairs. She could not reach her navel with her hands by one and a half feet, and was so emaciated that without her tumor companion she would hardly make a shadow." The volume of fluid contained in Spohn's cyst was thirty-six gallons, Bullitt's contained thirty-four gallons. The average bathtub has a capacity of fifty-seven gallons.

The weight of the sac varies from 2.5 to 70 pounds, the larger sacs usually belonging to the multicystic type of tumor with its numerous subsidiary cysts.

The weight of the patient before operation in several of the larger cases was nearly 400 pounds. In Binkley's case it was 396 pounds, in Bullitt's "near 400," in Smith's 375 pounds. Spohn does not state the weight of his patient. Due to the patient's usual condition of emaciation, her weight after operation is frequently far less than that of the tumor. The most marked contrast is presented in Payot's seventeen-year-old girl who weighed 66 pounds after the removal of a 198-pound tumor.

Complications.—The enormous abdominal distention and the pressure effects of the great tumor mass gives rise to very characteristic deformities. The ribs are usually widely flaring, the xyphoid frequently standing almost at right angles to the body. The ilia flare widely. In Henley's case, the erectores spinae were greatly hypertrophied to support the enormous weight, forming two ropelike strands at either side of the vertebral column. Edema of the legs is present in almost all cases, edema of the lower part of the abdominal wall in very many. The skin of the abdominal wall is either hypertrophied and thickened by edema, or so distended that it is very thin and tense. The abdominal veins are usually very markedly distended, often being as much as 1 centimeter in diameter. Pressure ulcers are common, both on the legs and on the abdominal wall. Pressure atrophy of the

thigh muscles, where the tumor is in contact with them, is very frequent and with the massive edema below gives rise to a very peculiar picture, just after the tumor is removed.

The thoracic organs are always displaced upwards. The heart's apex impulse was frequently found in the third space. The liver and spleen were sometimes flattened. The ovary involved by the tumor was the right in 17 cases, the left in 13, both in 3, and not stated in 52. The condition of the other pelvic organs is not stated in many cases, as many of the reports are incomplete. The uterus showed complete prolapse in only 2 cases. Baldwin's 185-pound case was the mother of two children, Sauligoux's 100-pound case was an unmarried girl of fifteen. In the series of 103 cases between 60 and 100 pounds, complete prolapse occurred 6 times, 2 times in nulliparas, and partial prolapse 2 times, once in a nullipara. The uterus was infantile in a number of cases. In the cases past the menopause it showed senile atrophy. Coincident myomata of the uterus were noted in 3 cases. Buffett's 180-pound unilocular cyst of the left ovary had also a subperitoneal fibroid weighing 36 pounds.

In 42 cases, the type of ovarian pathology is not stated. In 35 cases, the cysts were multilocular, probably of the pseudomucinous type. In 6 cases, they were unilocular. There was 1 dermoid weighing 100 pounds. In this case, the other ovary also contained a dermoid. There was 1 parovarian cyst of the left broad ligament weighing 105 pounds. There were 2 papillary cysts. One weighed 154 pounds. The patient recovered from the immediate results of the operation but died three months later of generalized abdominal metastases. The other weighed 125 pounds. This patient was discharged well on the twenty-sixth day following her operation, but her later history is not stated.

Type of Fluid.—The type of fluid was usually gelatinous in the multicystic tumors. As is usual in pseudomucinous cysts, the color and consistency frequently varied markedly in the different chambers, from a light greenish to a dark chocolate or even black. The monocysts usually contained thin, clear fluid.

Adhesions are of much importance in the operative technic, and rendered many of the operations extremely difficult. In 37 cases, the presence or absence of adhesions is not mentioned. In 3, it is definitely stated that there were no adhesions. Twenty-six cases had parietal adhesions, including adhesions to the diaphragm. In 5 cases the location of adhesions is not mentioned. Four had visceral, 12 had both visceral and parietal. The visceral adhesions included both large and small intestine, omentum, stomach, liver, gall-bladder, uterus and urinary bladder.

Symptomatology.—The symptomatology of these cases is that due to pressure and the mechanical inconvenience because of the size of the tumor. Many had no complaint except the latter. Many even

of the larger cases had been able to get about or even to perform their housework, until a few months before the time they came under observation. In the later stages, however, their condition was most deplorable. They became bedridden and entirely helpless, or possibly able to get about only on all fours. Most of them, because of dyspnea, were unable to lie flat; some had to sit up in a chair continually. Emaciation is constantly present, many have nausea and vomiting. Palpitation is a frequent symptom. Constipation is present in many cases. Oliguria and dysuria are frequent. Pain is a rare complaint. A number of cases had pain early while the tumor was yet small, although it disappeared later when the tumor reached large dimensions. The duration of symptoms is difficult to obtain. The symptoms are usually so vague and develop so gradually that the patient cannot state definitely when they began. The duration of the tumor is mentioned in 47 cases. It varied from ten months to twenty-one years.

Age.—In 31 cases, the age of the patient is not stated. There were 3 cases between ten and twenty years, 12 between twenty and thirty, 6 between thirty and forty, 15 between forty and fifty, 15 between fifty and sixty, 3 between sixty and seventy, 2 between seventy and eighty—a remarkably high proportion in women past the period of active sexual life.

The number of pregnancies is mentioned in 38 cases. Five were single, 10 were married but sterile, 6 had had one child, 11 several, 6 had had many; of these 2 had had fifteen children. The menstrual history is given in only 33 instances, whether because such a large proportion of tumors occur after the menopause is hard to state. One patient of fifteen years had never menstruated. A patient of seventeen had had three of four periods when fourteen years of age and none later. Eleven state that the tumor developed some years after the menopause. Five had had amenorrhea of three months to two years' duration before the time of the menopause. One had a very short interval between periods. In 4 the menses were undisturbed.

Prognosis.—The prognosis in these large tumors, whether without or with operation, is extremely serious. The outcome was not stated in 24 cases of this series, mostly early cases before the days of operations. Three were operated. Presumably all died, since there is no note to the contrary. In 12 cases, a fatal outcome without operation is recorded. Fifteen cases died following operation, 9 within a few hours, 5 later, in 1 the time of death is not stated. Shock is given as the cause of death in the earlier cases. Hemorrhage is not mentioned in any case as a cause of death, but the results of post-mortem examinations are not recorded. The cause of death in 2 cases which died on the second day is also given as shock; 1 on the sixth day as "exhaustion"; 1 on the seventh day as intestinal obstruction, 1 on the thirty-seventh day as sepsis. In this latter case, marsupialization was

done, the only case in this series where this procedure was applied. Immediate recovery was recorded in 36 cases, of these one died one month after operation, of pneumonia, apparently without relation to the operation. One died in three months from metastases following the removal of a papillary cyst. One died in six years of pulmonary cancer, but the type of ovarian pathology in this case is not recorded.

The percentage of recovery of all cases in the series was 41.4 per cent; of the operated cases, 71 per cent; of the cases over 175 pounds, 30 per cent recovered, of those operated 55 per cent. The prognosis in women with the larger tumors was much worse than the smaller. Though the death rate of operative cases since 1900 has not decreased notably, 73 per cent recovering, the total recovery rate is much higher, 59 per cent, since a larger proportion of cases were operated.

Although the outcome in cases not operated is usually death within a comparatively few years, it is remarkable how long such a patient may occasionally live in comparative comfort with frequent tapplings. The case of Martineau long stood as a classic. The dried cyst wall is preserved in the Museum of the Royal College of Surgeons. "The patient was twenty-seven years old when the disease commenced after a miscarriage with her first child. Between the years of 1757 and August, 1783, when she died, she was tapped eighty times, and in these operations there were altogether removed from her 6,631 pints of fluid or upwards of thirteen hogsheads. One hundred and eight pints was the largest quantity ever taken away at one time. She was never tapped more than five times in one year, and the largest quantity in one year was four hundred and ninety-five pints."

A far more remarkable case, however, is reported in recent years by Ashby. This patient first applied for treatment to Dr. J. L. Atlee, of Pennsylvania, in November, 1861. He removed thirty-two pints of fluid, and each year thereafter until 1885 the same quantity was removed. In 1880 Dr. Atlee urged ovariectomy, but after examination concluded it was too dangerous and resumed simple evacuation. Beginning March, 1885, it was necessary to tap more frequently, five times; in 1886, nine times; in 1887, eleven times; in 1888, sixteen times; from then until 1896, eighty-eight times, and then every three or four weeks. By 1903 her vitality was so lowered that an ovariectomy was advised as the only means of saving life. The patient had been tapped two hundred and sixty-nine times in forty-two years and two thousand one hundred and twelve gallons, or nearly seventeen thousand pints, or more than thirty-three hogsheads of fluid had been withdrawn. Operation was performed on November 11, 1903. An area of abdominal wall 4 by 6 inches was excised, the point of entrance for the numerous trocar wounds. The wall here was two and a half inches thick. Pedicle attaching the tumor to the uterus was very small, the sac was easily detached after the abdominal walls had been cut away. The tumor had obtained nourishment through its attachment to the

wall. The patient also had general miliary tuberculosis of the peritoneum. Her recovery was uneventful. One year later her left breast was removed because of a tumor. She had gained twenty pounds, and was in excellent health.

Vance's case was tapped one hundred and eighty-four times in forty-six years, and finally died of exhaustion aged eighty, after twenty-two thousand pounds of fluid had been removed from her. Other less remarkable cases in which from five hundred to six thousand pounds of fluid were removed by repeated tapplings over three to ten years are reported by Griffin, Shands, Falckner, Mead, Gilliam, Brown, Pagenstecher, Souligoux, Lee, Helmuth and Neal.

The post-operative condition in the cases which recovered is of some interest. Pain in the ribs is a frequent complaint due to the sudden relief of tension. There is frequently a diuresis beginning at the third or fourth day, with a disappearance of the edema.

There is a peculiar deformity due to the marked flaring of the ribs. In one case it was stated that, immediately after the operation, one could reach up through the lax abdominal wall and touch the under surface of the third rib. It is remarkable how soon after operation the deformity disappeared. One case was practically normal in four weeks. Difficulty in walking, and in maintaining balance is often mentioned in the early convalescence.

Due probably to the poor condition of the patients, a plastic operation to strengthen the abdominal wall was not attempted in any case with a tumor over 100 pounds, though it is mentioned in several cases weighing between 60 and 100 pounds. It was occasionally a difficult matter to dispose of the folds of skin to prevent maceration. Usually this was accomplished by the interposition of folds of cotton or gauze. Visceroptosis is not mentioned in any of the reports which state the later condition of the patient (13 cases). Several state definitely that the abdominal wall was firm; sometimes with considerable fat. A number of the patients were doing hard work within six months or a year later.

Résumé of Cases.—The accompanying table gives the cases weighing over 100 pounds. Short résumés of the cases over 200 pounds should be of interest.

Spohn's case—328 pounds, reported from Texas in 1905. Mrs. G., age forty-three years, children seven. Duration of disease, several years, numerous tapplings; 30 gallons of gelatinous fluid removed with small trocar during week immediately preceding operation; only six gallons present at time of operation. Multicystic tumor left ovary. Sac weighed 40 pounds. Recovery.

Barlowe—298 pounds, reported from Kentucky, 1846. Patient bed-ridden for long time, semireclining with shoulders much elevated because of dyspnea. From acetabulum across umbilicus, 6 feet, 6 inches. During three days, 19.5 gallons, which equals 176 pounds of

fluid removed. Patient died of exhaustion next day. At autopsy, 72 pounds of fluid and 50 pounds of wall removed, consisting of cysts size of lemon to child's head. Tumor originated in left ovary—nowhere adherent.

Bullitt—245 pounds, Kentucky, 1897. Patient age thirty-seven years, children, one. Tumor present many years. Operation arranged eight years previously but courage failed. Last one and a half years could rest only sitting. Dyspnea and weakness. Circumference of abdomen at navel, 79 inches. Twenty-four gallons of fluid removed at operation. Extensive parietal and visceral adhesions. Multilocular cyst. Died of intestinal obstruction seventh day.

Tuffier—235 pounds, France, 1906. Patient age seventy years, children, one, age forty-seven years. No history of pelvic trouble. Menopause at forty. Tumor for six years. Gradual general enlargement of abdomen without change of health or inconvenience. Bed-ridden for one year with dyspnea and palpitation. Cyst drained 94 liters fluid first operation, removed three weeks later. Uneventful recovery with later complete restoration abdominal wall and thorax to normal.

Binkley—225 pounds, Chicago, 1897. Fluid in tumor weighed 175 pounds, solid portion 50 pounds. Weight of patient before operation, 396 pounds. Case terminated fatally because of too rapid delivery of fluid. Tumor very heavy, thick-walled with numerous adhesions, separated with great difficulty.

Ward—222 pounds, California, 1907. Patient age forty-seven years, children 3. Tumor present seventeen years, catamenia regular until forty-five. Weight before operation, 309.5, 24 gallons fluid. Circumference umbilicus, 6 feet 10 inches. Multilocular cyst right ovary with firm and dense adhesions to liver, gall-bladder, spleen, intestines and peritoneum. Death due to shock one hour post-operative.

Martineau—216 pounds, England, 1784. Case cited without details by Gallez.

Adelmann—214 pounds, Germany. Case cited without details by Gallez.

Pfäehler—202 pounds, Switzerland. Patient age forty-two years; tumor five years; able to do housework until one year previous. For several months could only lie on bed or kneel. Emaciation, dyspnea, palpitation, edema legs and labia, constipation. Circumference abdomen 170 centimeters. Operation, 74 liters fluid removed—cyst four chambers left ovary—adherent to parietal peritoneum and diaphragm. Weight tumor 97 kilograms, of patient 47 kilograms. Recovery.

Garcelon—202 pounds, American. Patient age twenty-eight years, normal weight 115 pounds, circumference at umbilicus, 69 inches. Both ovaries diseased. Fluid 132 pounds, sac 70 pounds. Patient never rallied, died two days post-operative.

MAMMOTH OVARIAN TUMORS

Weight reported (lbs.)	Author	Locality	Date discovered	Age	Outcome
328	Spohn	Texas	1905	43	Recovery
298	Barlowe	Kentucky	1846	?	Death without operation
245	Bullitt	Kentucky	1897	37	Death seven days after operation
235(?)	Tuffier	France	1906	70	Recovery
225	Binkley	Illinois	1896	?	Death at operation
222	Ward	California	1907	47	Death one hour after operation
216	Martineau	England	1784	?	Not stated—without operation(?)
214	Adelmann	Germany	1816	?	Not stated—without operation(?)
202	Pfaehler	Switzerland	1904	42	Recovery
202	Garcelon	America	1882	28	Death two days after operation
198	Payot	France	1893	17	Recovery
192	Smith	Massachusetts	1906	42	Death twenty-four hours post-operative
185	Baldwin	England	1900	59	Death without operation
182.5	Reifsnyder	China	1895	25	Recovery
180	Buffett	Rouen	1887	?	Death without operation
160+(20)?	Kimball	Massachusetts	1872	?	Operation not completed
176+	Gallo	Argentina	1919	?	?—probably death without operation
176	Gilliam	New York	1899	45	Operated—result not stated
175+	Fay	Tennessee	1908	54	Death one month after operation
175(?)	Mudd	St. Louis	1884	?	Not operated
166	Spohn	Texas	?	?	Death at operation
165	Maritan	Marseilles	1893	?	Recovery
164	Harley	India	1921	40	Death next day after operation
160	Cordier	Missouri	1905	?	Death few hours after operation
160	Gaitskell	England	1873	?	?
160	Davis	Pennsylvania	1893	55	Death six hours after operation
160	Franz	Germany	1916	50	Recovery
154	Cullingsworth	England	1891	45	Death at operation
154(?)	Brunner	Germany	1901	44	Death three months after operation—metastases
152	Squire	Massachusetts	1870	65	Death without operation
150	Tozetti	Italy	1897	?	?
149	Briddon	New York	1890	36	Death twelve hours after operation
148+	Peaslee	Massachusetts	1860	21	?
147	Phoebler (quoted by Pelliza)		?	?	?
146	Rodenstein	America	1878	45	Death without operation
140	Larkins	India	1912	62	Death without operation
140	Peaslee	America	1872	?	?
140+	Aquino	India	1895	40	Death without operation
140	Gallez	France	1873	?	?—probably death without operation
139½	Edmonds	China	1915	?	Recovery

MAMMOTH OVARIAN TUMORS—*Continued*

Weight reported (lbs.)	Author	Locality	Date discovered	Age	Outcome
134½	Idazewski	Germany	1903	63	Death thirty-seven days
132	Poncet	France	1889	57	?
132	McGillicuddy	America	1825	28	?
130	Caballero	Argentina	1914	22	?
129+	Mann	Holland	1888	?	Recovery
128	Unterberger	Germany	1898	?	Recovery
128	Wenzel	Vienna	1908	58	Recovery
125(?)	Lynds	Michigan	1898	54	Recovery
125(?)	Atlee	America	1871	33	Death three hours
125	Estes	Pennsylvania	1887	40	Recovery
125	Wells	England	1873	53	Recovery
		(Brazil)			
121	Caballero	Argentina	1906	52	Recovery
120(?)	Ponchon	Brussels	1881	58	Recovery
120	Keith	Scotland	1879	?	Recovery
120	Martineau	England	1784	?	?—death without operation
119	Neal	Kentucky	1880	33	Death without operation
119	Yondell (quoted Cartledge)		?	?	?
116	Horsley	America	1911	33	Recovery
116	Kelly	Maryland	1885	42	Recovery
116	Brown	England	1849	31	Death without operation
114	Falckner	Switzerland	1893	53	Recovery
112	St. Toth	Germany	1902	58	Recovery
112	Samson	England	1815	?	?—death without operation
112	Gallez	France	1873	?	?—death without operation
112	Goodell	Pennsylvania	1882	31	Recovery
111	Cartledge	Kentucky	1891	30	Recovery
111	Keen	Pennsylvania	1893	15	Recovery
111	Knight	Pennsylvania	1912	?	Recovery
110	Rouffart	Belgium	1900	59	Recovery
110(?)	West	England	1851	24	Death
110	Potvin	Belgium	1900	59	Recovery
106	Gibb	London	1855	31	Death without operation
106+	Peaslee	America	1860	?	?—probably death without operation
105	Mayo-Robson	England	1884	37	Recovery
105	Homans	Massachusetts	1884	?	Recovery
104	Skutsch	Germany	1904	53	Recovery
102+	Bosch	Germany	1873	?	?—death without operation
102	Van den Bosch	America	1883	?	?—death without operation
100	Burford	England	1892	55	Recovery
100	Fussell	Pennsylvania	1901	47	Death few hours after operation
100	Keith	England	1895	55	Good recovery
100	Kelly	Maryland	1886	?	?
80+20	Peaslee	America	1849	28	Death without operation
100?	Wörner	Germany	1899	65	Death without operation
100+	Wörner	Germany	1899	76	Recovery
100	Willi	Germany	1873	?	?—death without operation

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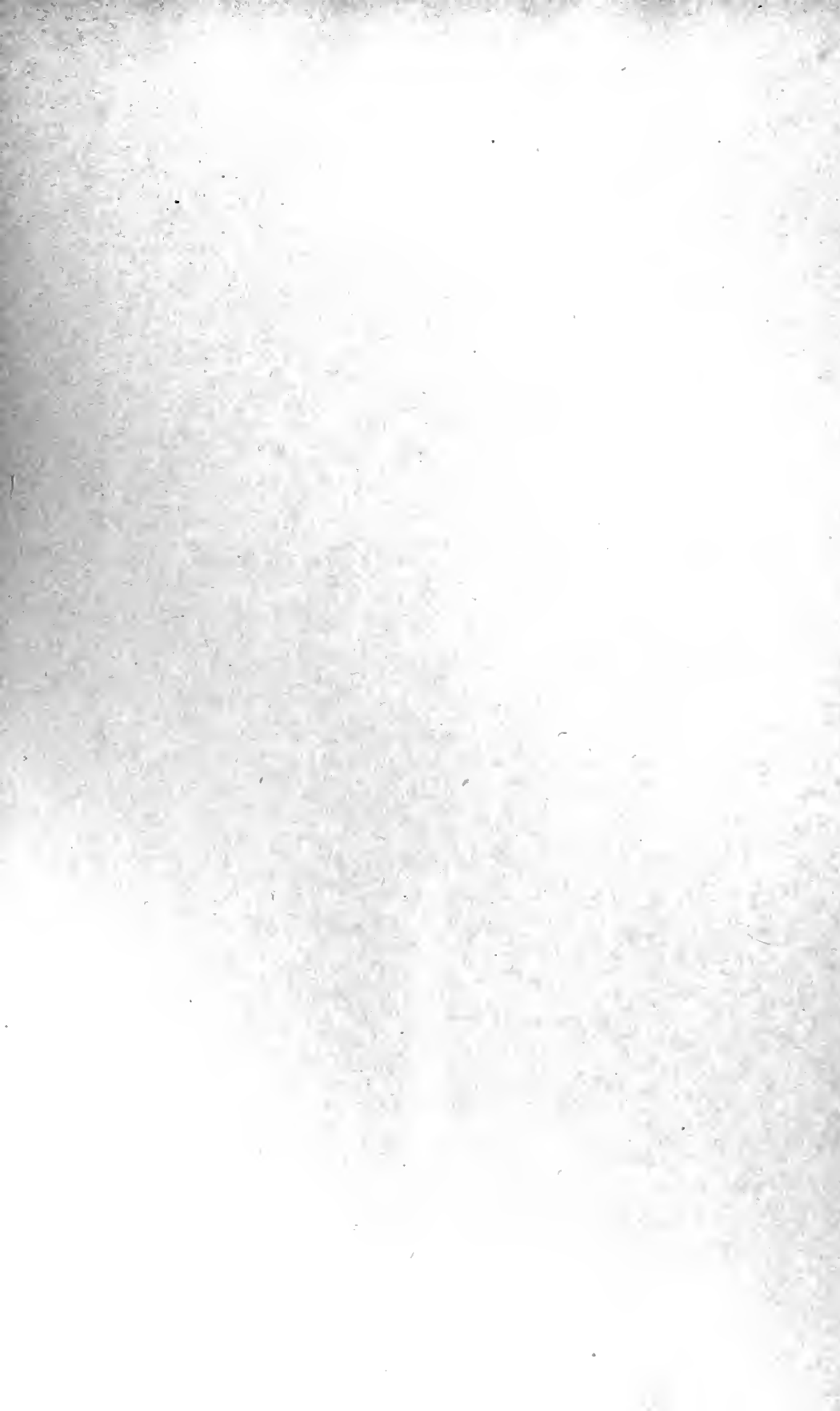
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